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DOGS VS. CATS

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INTERNAL CLOCKS

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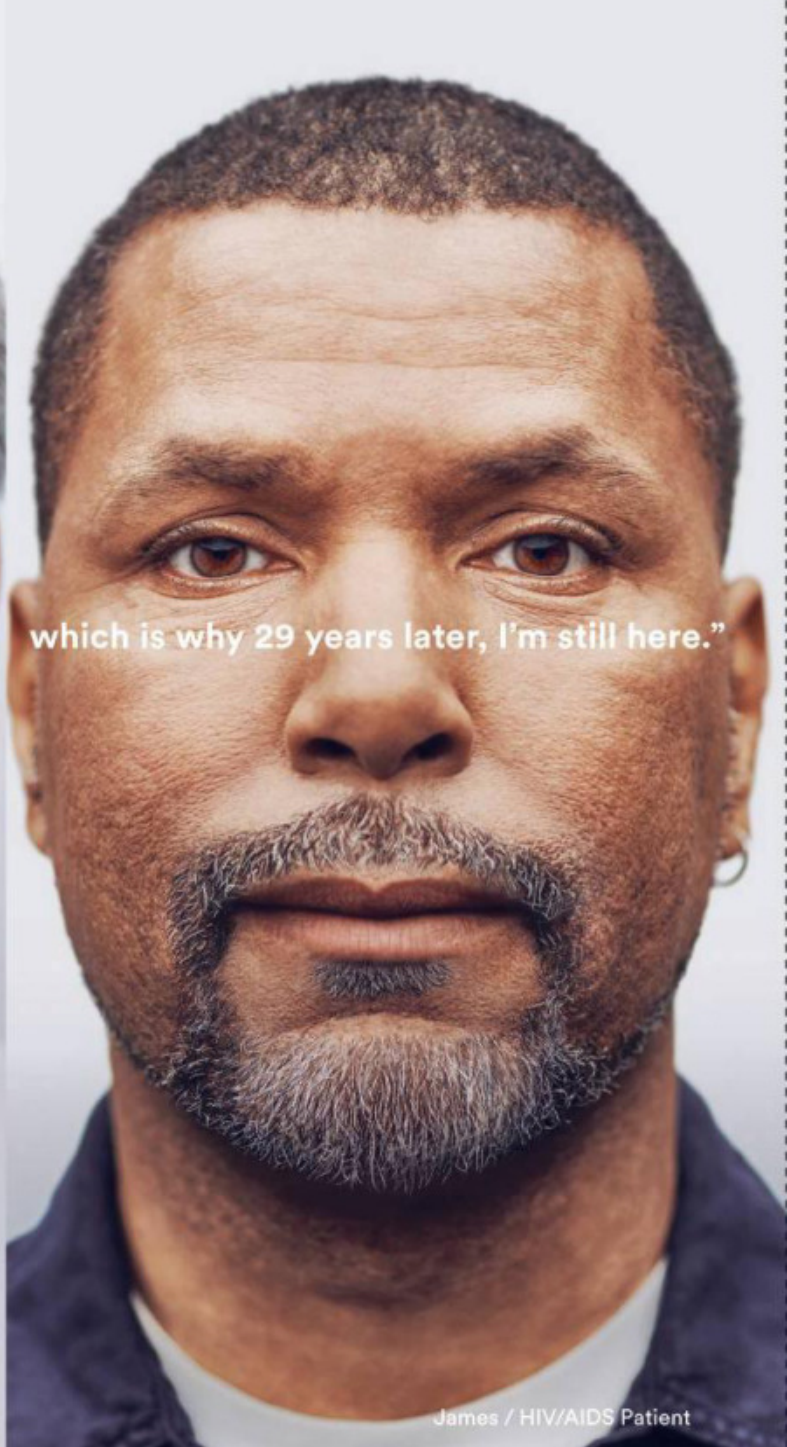
SCIENTIFIC AMERICAN

CROSSING
THE
QUANTUM
DIVIDE

Where is the
line between
the quantum
and classical
worlds?



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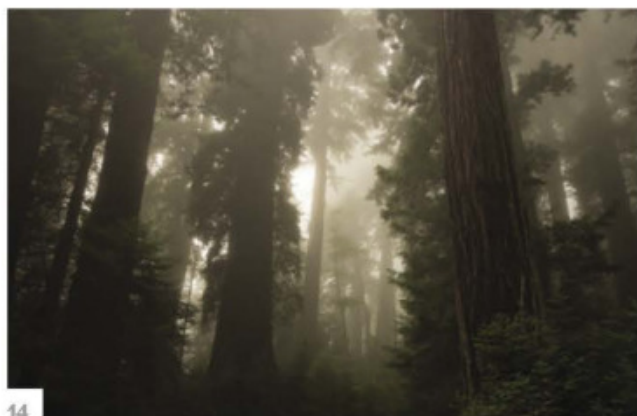
As mosquito-borne diseases spread, scientists are fighting back with new poisons, traps and genetic engineering techniques. *By Dan Strickman*



ON THE COVER

The subatomic world seems to obey different rules than those that govern our "normal," macroscale reality. Scientists hope to understand what divides these two realms with laboratory experiments that will seek to put macroscopic objects in quantum states.

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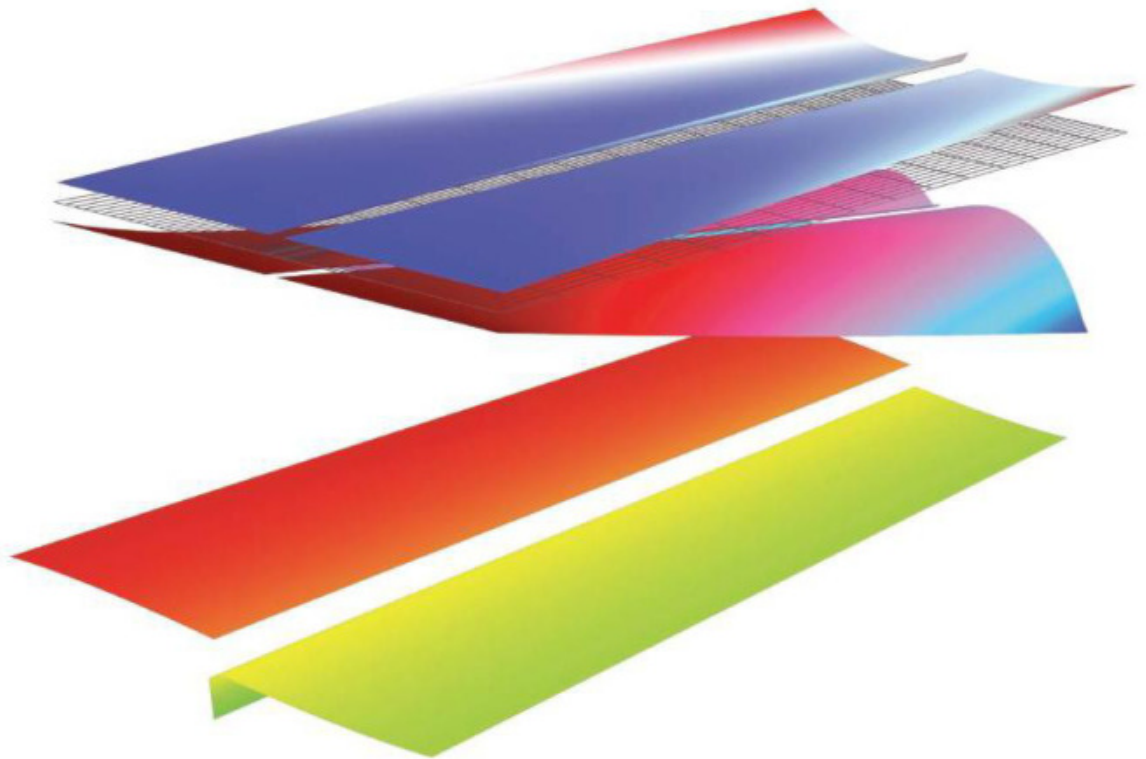
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enough for the power grid.



Visualization of the concentration of V^{3+} and VO^{2+} ions (top), V^{2+} and VO_2^{+} ions (middle), and electrolyte potential (bottom) in a vanadium redox flow battery.

When developing rechargeable batteries for the power grid, vanadium is a stronger contender than lithium. Advantages include scalability, longer and more consistent operation lifetimes, safety, and the ability to fill in the gaps when wind or solar power suffers intermittency issues. But vanadium redox flow batteries (VRFBs) do bring shortcomings of their own. Engineers looking to improve grid energy storage and reliability often start by optimizing VRFB designs.

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Mariette DiChristina is editor in chief of *Scientific American*. Follow her on Twitter @mdichristina

Barriers between Realities

We may think we have an ability to be fair and impartial—to make decisions and judgments based on the weight of evidence. But unfortunately, we humans are all irrational. When faced with an overwhelming amount of information, our brains take shortcuts; instead of taking time to analyze, we may accept a group decision or a trusted expert. Worse, even when we have time to consider our decisions, we prefer to interpret the evidence to fit our preexisting beliefs, called confirmation bias. And even if we can clear the first two hurdles, we may fall prey to social motivations. We may accept beliefs that seem more likely to improve personal status, or that conform to the views of a political party, or that even help us find a partner.

Starting on page 36, we take a look at “The Science of Anti-science Thinking,” co-authored by researchers Douglas T. Kenrick, Adam B. Cohen, Steven L. Neuberg and Robert B. Cialdini. What happens when our irrational tendencies encounter the process of science, which promises an unvarnished view of reality,

based on testing and collected evidence—on facts? Perhaps unsurprisingly, we celebrate the fruits of research when the process yields something we value—a cure for a disease, say, or the latest smartphone. But what if we don’t like what we hear? We reject it.

Sadly for us, some problems, such as global climate change, mean that we can’t dally forever. On the bright side, psychologists have developed strategies—such as a change of perspective—to help counteract our natural inclinations. It’s a welcome dose of optimism for a sometimes puzzling world.

Speaking of confounding topics, how about the strange, probabilistic quantum-mechanical world versus our everyday “classical”

world, where everything seems to be hard and fast? In this issue’s cover story, “Crossing the Quantum Divide,” science journalist Tim Folger lays out upcoming efforts by physicists to explore where one realm passes into the other. Turn to page 28.

How the body’s cycles crossed the line from folk medicine into modern science is the topic of “The Clocks within Our Cells,” by science writer and essayist Veronique Greenwood. Beginning on page 50, she describes an emerging field called chronomedicine, which is testing timed treatments of diseases such as cancer and rheumatoid arthritis. Someday personalized monitoring of circadian rhythms may support different treatment times for each of us.

As always, if you feel it’s time to surmount the border between editors and readers, please do communicate with us about the stories in this issue. We welcome your responses. ■



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March 2018

SIDE-EFFECTIVE USE

Claudia Wallis's account of how her opinion regarding treatment options for osteoporosis has changed in "A Perfectly Avoidable Crisis" [The Science of Health] was interesting. But I was disappointed that she did not back up her claim that "new drugs have emerged that do not have the same risks" of osteonecrosis of the jaw and atypical femoral fracture that oral bisphosphonates do. I would have appreciated knowing the names of those drugs and at least a little something about the research that suggests their greater safety. I'm sure that rather than accepting even a small risk of devastating side effects, most women with osteoporosis would opt for a "risk-free" treatment—if such a thing existed—or even one with side effects that are less potentially severe.

ELIZABETH HUTCHISON BERNARD
Scottsdale, Ariz.

WALLIS REPLIES: *Hutchison Bernard raises an important question that I didn't have room to address. Not every drug for osteoporosis carries these specific risks. Some work by a different mechanism than the bisphosphonates and have a different profile of side effects. Teriparatide and abaloparatide, for instance, are injectables that appear to build bone rather than just slowing bone turnover. But they, too, involve certain risks. Moreover, patients who take them are usually switched over*

"The question is not whether a system in which blood or skin cells are used in place of sperm or eggs can be perfect but whether it can be better than the alternative."

JOHN ORLANDO WILLISTON, VT.

to bisphosphonates after 18 to 24 months to maintain bone density. For some patients, hormone replacement therapy or the related drug raloxifene are good options, although they have risks as well. Bottom line: treatment for osteoporosis should be tailored to the individual patient, based on a careful evaluation and discussion with an endocrinologist or another specialist.

REPRODUCTION RISK

In "The Means of Reproduction," Karen Weintraub discusses fertility research on converting blood or skin cells into viable sperm and eggs. She states that Marcy Darnovsky of the Center for Genetics and Society "does not think that lab-generated germ cells could ever be safe enough to justify their risks" and quotes her as saying this is because "it's likely to be extremely biologically risky for any resulting children." Darnovsky then notes that many cloned mammalian embryos fail to develop and that some have been born with birth defects.

But embryos frequently fail to develop in regular reproduction, and children are born with health problems in regular reproduction as well. The question is not whether a system in which blood or skin cells are used in place of sperm or eggs can be perfect but whether it can be better than the alternative. At some point, it might even be safer than regular reproduction by eliminating birth defects such as Down syndrome. People might even someday blame parents who choose traditional reproduction over the safer sci-

entific methods for carelessly subjecting their children to greater risk.

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SUPERHEAVY EMITTER

In "Island of Heavyweights," Christoph E. Düllmann and Michael Block discuss efforts to create superheavy elements that would last for minutes or longer before decaying, forming an "island of stability" on the periodic table.

I would think superheavy isotopes near the island of stability would be created by neutron star collisions, which excel at creating heavy, neutron-rich isotopes. Might superheavy elements be detectable in the debris of neutron star collisions, such as the one seen last year? Was uranium detected or inferred in that collision's debris?

DAVID LAMBERT San Jose, Calif.

DÜLLMANN REPLIES: *The question of whether superheavy elements are formed in processes occurring in nature is among the most interesting aspects of the field and has not yet been conclusively answered. An open question is how the heaviest nuclei created in astrophysical phenomena decay. If they decay by spontaneous fission—that is, by disintegrating into two lighter fragments—access to very long-lived nuclei at or near the center of the island of stability is blocked. If, on the other hand, they are stable enough against spontaneous fission that other decay modes, such as beta decay, dominate, a pathway to the island may be available. Hence, studying the nuclear structure and stability of the heaviest elements is an important part of superheavy element research. Of special interest are the most neutron-rich nuclei, as astrophysical events proceed in neutron-rich environments.*

As for the recently observed neutron star collision: individual elements were not identified. The detected optical signature is best explained by the formation of very heavy elements, but scientists did not measure an observable tied specifically to uranium.

IMPERMANENT REVOLUTION

Andrea Gawrylewski's review of *The Wizard and the Prophet*, by Charles C. Mann [Recommended], misrepresents Norman Borlaug, who helped to bring about the

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green revolution, as thinking “technology would find a way to save us.”

Borlaug was well aware that the green revolution didn’t address the root of the problem. In the lecture he gave when he received the Nobel Peace Prize in 1970, he said, “The green revolution has won a temporary success in man’s war against hunger and deprivation.... If fully implemented, the revolution can provide sufficient food for sustenance during the next three decades. But the frightening power of human reproduction must also be curbed; otherwise the success of the green revolution will be ephemeral only.” He therefore saw the green revolution simply as a stop-gap while humanity, he hoped, got its act together on the real problem.

ROGER PLENTY *Stroud, England*

EVOLVING UNDERSTANDING

In “Alvy’s Error and the Meaning of Life” [Skeptic, February 2018], Michael Shermer makes his own teleological error by ascribing design to evolution: “We are sentient beings designed by evolution to survive and flourish in the teeth of entropy and death.” There is no plan in the unfolding of evolution, but there is great mystery in carbon becoming aware of the universe and using words to describe its grandeur.

JAMES WADE *Dallas, Tex.*

SHERMER REPLIES: Wade is correct in the sense of top-down goal-directed evolution, but Charles Darwin’s genius was to show how evolution can produce the illusion of top-down design from the bottom-up process of natural selection. Functional adaptations are “designed” features of nature: wings are designed to fly; eyes are designed to see. Carbon atoms are not aware of anything. But when combined to help build complex protein chains that form cells, some of which are neurons that generate thoughts in brains, awareness of the cosmos and even self-awareness are possible, given time. It would seem that 4.6 billion years is sufficient, at least on this planet. The next big discovery will be where else this has happened in the cosmos.

ERRATUM

“Quick Hits,” by Yasemin Saplakoglu [Advances], incorrectly referred to ticks as insects. They are arachnids.

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Safe Injection Facilities Save Lives

To fight the opioid crisis, let users shoot up under medical supervision

By the Editors

Annual opioid fatalities have now surpassed the yearly number of deaths from AIDS at the height of that epidemic in the mid-1990s. In 2016 drug overdose deaths numbered 63,000, more than the U.S. death toll from the entire Vietnam War. The trend is terrifying: the problem is getting worse each year.

Cities and states reeling from opioid deaths need to give serious consideration to setting up safe injection rooms, which could significantly reduce fatalities. These are places where a drug user can go to consume illegal drugs under the supervision of health workers. They have been used in Europe, Canada and Australia for decades, and evidence and experience have shown that they are very effective. This may not seem like an obvious way to fight an abuse epidemic, but few other options exist. In the U.S., many cities' efforts to establish such sites have stalled, but now multiple cities have plans to open the country's first officially sanctioned injection sites. Philadelphia expects to do so in 2019. San Francisco, too, hopes to overcome legal and siting obstacles and open its first facilities this year. New York City's mayor has also endorsed setting up multiple sites at current needle-exchange programs.

Misuse of prescription opioids such as OxyContin is inextricably linked with that of street drugs such as heroin. Nearly half of young people who inject heroin started by abusing prescription drugs. Then they turned to the cheaper, more readily available alternative. The path from pills to needles has meant that U.S. deaths from heroin have increased by a factor of five since 2010, topping 15,000 people in 2016. And the toll is continuing to climb as people overdose on heroin laced with fentanyl, a synthetic opioid that makes heroin much more potent—and much deadlier.

That is where safe injection sites come in. If someone overdoses at one of more than 90 such locations in Europe and elsewhere, a health worker or other first responder quickly administers an antidote. The facilities have also proved they can reduce the transmission of blood-borne infections, partly through needle exchanges. Moreover, they can save money: in San Francisco, for example, one analysis concluded that for every dollar spent on supervised sites, \$2.33 in emergency medical, law enforcement and other costs would be reduced, producing a yearly net savings of \$3.5 million.

The evidence for increased safety is compelling. At Insite in Vancouver, B.C., there was a 35 percent reduction in fatal overdoses in the area around the facility, compared with a 9.3 percent reduction



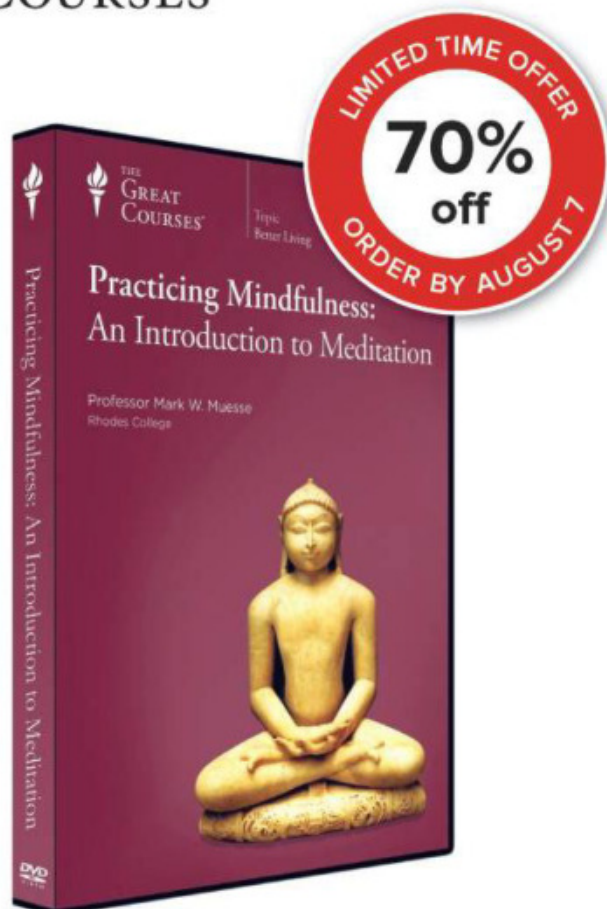
in other parts of the city that may have had other interventions. People who used Insite were also much less likely to share needles than those who shot up in unsupervised places. And of the 8,040 people who visited the facility in 2016, 517 were referred to addiction treatment, and more than a third of them completed it.

Critics argue, correctly, that injection sites are not a perfect solution. Our country also needs more drug-treatment beds and counseling options; medication assistance to help with drug withdrawal; and other evidence-based care to alleviate the crisis. Safe sites also work best in places where drug use is centralized, such as in specific urban neighborhoods rather than rural areas. And of course, they are controversial because they require officials to tacitly accept illegal drug use.

That is why no American city has yet cleared the necessary hurdles to proceed with establishing an injection site. In addition to San Francisco and Philadelphia, Denver has considered this option. Seattle, too, has called for two safe consumption rooms and has even set aside funds to support them, but its effort has been mired in legal battles. Federal law currently makes it illegal to use nonprescribed opiates and opioids, so Philadelphia officials have said they would not fund or operate such a facility. They would instead encourage private efforts to open one—which would perhaps provide slightly more legal distance than if they were to finance and manage it themselves. Still, the U.S. Department of Justice could choose to prosecute the city for endorsing the move.

But if a site in Philadelphia, San Francisco or elsewhere does get off the ground, it could at last pave the way for other cities to follow suit, giving communities new hope that the rising death toll from the opioid crisis might finally begin to recede. ■

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Auto Mileage Rollback Is a Sick Idea

The current EPA rules are better for our wallets and our health

By Rob Jackson

Seven years ago representatives from General Motors, Ford, Chrysler and other car manufacturers joined President Barack Obama to announce historic new vehicle mileage standards. The industry-supported targets would have doubled the fuel efficiency of cars and light trucks in the U.S. to 54.5 miles per gallon by 2025.

But in April the Environmental Protection Agency announced plans to roll back part or all of the new standards, saying they were “wrong” and based on “politically charged expediency.” Let me explain why this terrible idea should unify Republicans and Democrats in opposition. The rollback is going to harm us economically and hurt us physically.

The Obama-era standards made sense for many reasons, starting with our wallets. It is true that each vehicle would initially cost \$1,000 to \$2,000 more as manufacturers researched lighter materials and built stronger vehicles. In return, though, we would save about \$3,000 to \$5,000 in gas over the life of each vehicle, according to a 2016 report by Consumers Union. (Because gas prices were higher in 2011 and 2012, when the stan-



Rob Jackson chairs Stanford University's earth system science department and is a senior fellow at the Stanford Woods Institute for the Environment and the Precourt Institute for Energy.

dards were proposed, estimated savings back then were significantly higher—about \$8,000 per car. Prices have risen somewhat since 2016.) This research will also help auto companies compete internationally.

National security and trade deficits are also reasons to keep the existing standards. Despite a growing domestic oil industry, the U.S. imported more than 10 million barrels of oil daily last year, about a third of it coming from OPEC nations. Imports added almost \$100 billion to our trade deficit, sending hard-earned dollars to Canada, Saudi Arabia, Venezuela, Iraq and Colombia. Better gas mileage could eliminate half of our OPEC imports. It would also make our country safer and more energy-independent.

The biggest reason to support the fuel-efficiency standards, however, is the link between vehicle exhaust and human health. More than four in 10 Americans—some 134 million of us—live in regions with unhealthy particulate pollution and ozone in the air. That dirty air makes people sick and can even kill them. A 2013 study by the Massachusetts Institute of Technology estimated that about 200,000 Americans now die every year from air pollution. The number-one cause of those deaths—more than 50,000 of them—is air pollution from road traffic.

Air pollution, and smog in particular, is the reason California places so much emphasis on air-quality standards. The federal Clean Air Act gives the state the right to set its own standards for vehicles, pending approval by the EPA administrator. This arrangement is not new. It began with model-year 1969 vehicles. Every White House administration since then—Republican and Democrat—has approved waivers for California and allowed other states to follow California's lead.

Despite tremendous progress by companies and through targeted regulations, California still has the worst air quality in the country. According to the American Lung Association, the top four metropolitan areas for ozone pollution are those of Los Angeles, Bakersfield, Visalia and Fresno. Six of the top seven for year-round particle pollution are all in California, too. In case anyone thinks this is blue-state California's problem, think again. Air pollution is red-blue color-blind when it comes to making us sick. Other cities high on the pollution lists include Phoenix, Pittsburgh, Salt Lake City, Cleveland, Cincinnati, Dallas and my childhood home, Houston.

Here is what a rollback in mileage standards would mean: Thousands of Americans would die unnecessarily from cardiovascular and other diseases every year. Our elderly would face more bronchitis and emphysema. More children would develop asthma—a condition that, according to an estimate by the Centers for Disease Control and Prevention, affects more than one in 12. Millions of your sons and daughters have it. My son does, too.

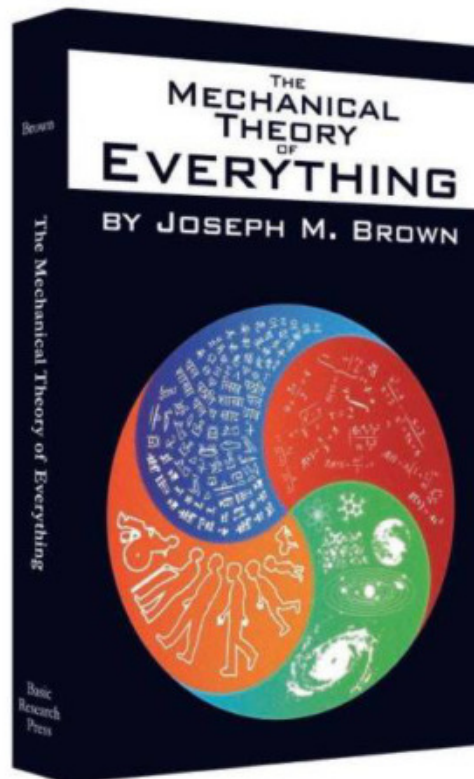
Rarely in my career have I seen a proposal more shortsighted and counterproductive than this one. Please say there is still time to change our minds. ■

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The Mechanical Theory of Everything.

The *Mechanical Theory of Everything* is the most remarkable book ever written on physical science. This book begins with the development of the five postulates for the positive integers and then outlines how scientific language (including logic) is evolved, outlines how the mathematics required to describe the universe is evolved, and then shows the all-pervading laws of mechanics which govern the behavior of everything physical in the universe. Next, the few basic physical postulates are developed from which observed physical results are derived. This entailed discovering the mechanism which organizes the chaotic background to make energy available, correcting Einstein's relativistic and gravitational theories, and showing that the universe is not expanding. In addition to showing how to derive physical science from language upward, the book shows what produces human aging.



Subsequent to the 2015 publication of *The Mechanical Theory of Everything*, we published in 2017 the booklet *Synopsis and Further Developments of the Mechanical Theory of Everything* which included our discovery of the origin of cosmic rays and the Newtonian derivation of the Schrödinger equation. This year, 2018, we published *The Fundamental Particles of Physics*, which reported our discovery of the structures of the unstable matter particles and the proof that parity is always conserved. This publication completed the derivation of all the basic observed physical phenomena in the universe. The three publications do it all. They are THE publications on science. Spend the time to master the three publications and you too will know for certain how the universe works. We warn you, though, these publications are not for the faint of heart.



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ADVANCES



Sedimentary rocks, such as those in the Grand Canyon, contain surprisingly high levels of nitrogen.

- Not all people are equally perceptive
- Using sound to trace a devastating fishing technique
- How to turn an ordinary wall into a smart one
- Parents invest more in some kids than others

GEOCHEMISTRY

Rocky Secret

A previously unknown source of nitrogen lies beneath our feet

Experts used to think nearly all nitrogen in soil came directly from the atmosphere, sequestered by microbes or dissolved in rain. But it turns out scientists have been overlooking another major source of this element, which is crucial to plant growth: up to a quarter of the nitrogen in soil and plants seeps out of bedrock, according to a study published in April in *Science*.

Apart from a few scattered studies, “the [research] community never thought to look at the rocks,” says lead study author Benjamin Z. Houlton, a global ecologist at the University of California, Davis. This discovery has implications beyond understanding the planet’s nitrogen cycle; it could also alter climate models. It suggests plants in certain areas may be able to grow faster and larger than previously thought and could thus absorb more carbon dioxide, Houlton says.

As global temperatures rise, calculating how much heat-trapping carbon dioxide plants soak up is becoming increasingly important. The exact amount remains uncertain, but Houlton notes that plants could provide “a little bit more of a cushion ... to store our carbon pollution.”

Previous research had examined the balance between how much nitrogen in sediments makes it to the mantle (the layer below the earth’s crust) and how much volcanoes release into the atmosphere



PAUL RUDAS/Getty Images

(which is 78 percent nitrogen). Beginning in the 1970s, a few studies showed that several types of sedimentary rock contain nitrogen from long-dead plants, algae and animals deposited on the ancient seafloor. A handful of papers suggested the element might leach into soil in certain places. But scientists did not follow up on these findings, and the amount of nitrogen released as rocks weather was thought to be insignificant. "It wasn't entering into the paradigm of how we think the nitrogen cycle works," Houlton says.

He and his colleagues published a study in 2011 in *Nature* finding that forest soils above sedimentary rock in parts of California contain 50 percent more nitrogen than in areas overlying igneous (volcanic) rock. They also found 42 percent more nitrogen in trees growing over sedimentary bedrock. Although the research suggested the element was making its way from rocks into soil and plants in a few specific areas, it did not show this to be a significant phenomenon worldwide.

In their new study, Houlton and his colleagues used California as a model geologic system because the state contains most of the planet's rock types. They measured nitrogen levels in nearly 1,000 Californian samples and in others from around the globe. They then developed a computer model to calculate how quickly the earth's



Redwood forests grow over nitrogen-rich soils and rocks, which helps to explain why they reach such massive sizes.

rocks break down and release nitrogen into the soil.

Nitrogen liberated by weathering processes eventually makes its way to the ocean, where it is deposited in rocks as they form on the seafloor. Tectonic plate movement lifts up the rocks; they degrade and release their nitrogen, which gets absorbed by plants and animals and trapped in rocks again—perpetuating the cycle. Weathering can involve both physical breakdown—which is accelerated when rocks are thrust upward and exposed to the elements as mountain ranges—and chemical dissolution, such as

when acidic rainwater reacts with compounds in rocks.

William Schlesinger, a biogeochemist at the Cary Institute of Ecosystem Studies in Millbrook, N.Y., who was not involved in the study, says he once measured substantial nitrogen levels in rocks but did not "put two and two together." He had assumed this was not a widespread or important source of the soil nutrient. But Schlesinger cautions against overinterpreting the significance of the new findings, noting that the amount of nitrogen entering soils via synthetic fertilizers dwarfs that from rocks. He thinks the discovery

ILLUSTRATION © DOANE GARY/IMAGES

PSYCHOLOGY

Eagle Eye

Not everyone has the same aptitude for observing detail

Our abilities to see things that appear fleetingly or in cluttered environments or outside our focus of attention are all determined by a single perceptual capacity trait that varies among people, a new study suggests. Researchers say these findings could one day help scientifically predict an individual's performance in jobs that rely on strong observational skills.

Psychologists Joshua Eayrs and Nilli Lavie of University College London tested participants on a range of visual tasks. One measured how well people could estimate the number of objects appearing on

a screen for a tenth of a second—a capacity known as subitizing. Others measured the ability to notice small differences between two real-world scenes; to detect a change at a screen's edge while focusing on the center; and to track multiple moving dots among static ones.

People who excelled at subitizing also tended to perform better on the other tasks, the team reported online in March in the *Journal of Experimental Psychology: Human Perception and Performance*. "This is the first study to establish a perceptual capacity trait," Lavie says. "It's an important ability, which [determines] how much information you can process when there's a lot of it around you."

Theoretically, performance on any task that relies on this perceptual ability (not just those studied) could predict perfor-



“The [research] community never thought to look at the rocks” as a source of nitrogen.

—Benjamin Z. Houlton,
University of California, Davis

should be incorporated into global models for nitrogen and carbon but adds, “I don’t think it’s going to rewrite our understanding of climate change.”

Nevertheless, the findings explain puzzlingly high nitrogen levels in some soils. “Our study helps to resolve that gap between what the observations were saying and what the models were predicting,” Houlton says. These results are especially important in considering massive, nitrogen-rich forests in Canada and Russia, many of which overlie sedimentary formations.

Houlton says that the new study used rather conservative measurements of nitrogen in rocks and that the actual quantity is probably higher than his team calculated. “Certainly humans and our activities have dramatically increased the amount of erosion,” which would boost nitrogen release through weathering, he says—and “we haven’t considered that in our study.”

—Doug Main

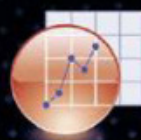
mance on any other. Lavie’s team also demonstrated that perceptual capacity is distinct from general cognitive ability and ruled out other possible factors such as varying levels of motivation.

The findings are interesting and plausible—but they are preliminary and need to be independently replicated in larger samples, says psychologist Matt Meier of Western Carolina University, who was not involved in the study.

The scientists say their work could help develop tests to screen potential employees for safety-critical jobs in demanding visual environments, such as air-traffic controllers, security guards or military personnel. Lavie says her team is already investigating whether measuring perceptual capacity can predict actual job performance in such roles.

—Simon Makin

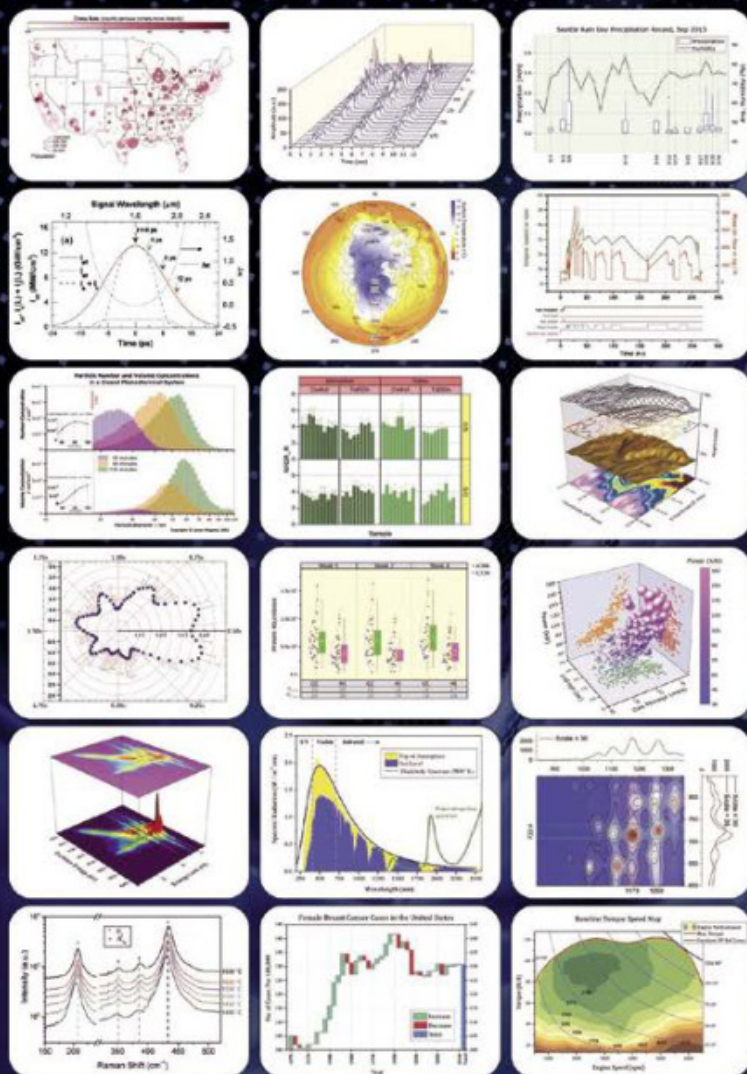
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SYNTHETIC BIOLOGY

Microbe Mystery

Engineered organism hints at the origins of bacteria and archaea

Billions of years ago the single-celled common ancestor of all life on earth split into bacteria and archaea, according to evolutionary theory. Now scientists have genetically engineered a microbe that combines features of both domains, offering insight into how this pivotal event occurred.

Bacteria and archaea are both unicellular organisms that lack nuclei, but they have distinct genetic and chemical makeups. Their cell membranes, for example, are made up of two different kinds of fatty molecules, known



as lipids. A long-standing hypothesis for the split between these domains is that their common ancestor's membrane contained both lipids, making it unstable and perhaps leaky—and less evolutionarily favorable.

Microbiologists in the Netherlands decided to test this notion by re-creating a primitive organism with a hybrid-lipid membrane. They spliced the gene for archaeal lipids into *Escherichia coli* bacteria, then modified the organisms' metabolism to boost production of molecules needed to make these lipids. The resulting *E. coli* strain had cell membranes containing up to

30 percent archaeal lipids and 70 percent bacterial ones, the researchers reported in April in the *Proceedings of the National Academy of Sciences USA*.

To the team's surprise, the new cells grew successfully, and the mixed membranes were stable. This "tips the scales toward other historical causes for the archaea-bacteria separation," says Eugene Koonin, an evolutionary and computational biologist at the National Institutes of Health, who edited the paper for the journal.

One alternative, says study co-author Arnold Driessen of the University of Groningen, is that there was not one common ancestor "but a mixture of multiple life-forms." A more bizarre scenario, Driessen says, is that the ancestor had no membrane but was "just a soup protected by clay particles." —Prachi Patel

STEVE GSCHEISSNER/Getty Images

ECOLOGY TECH

Fish Bombs

Gunshot-detection technology targets a devastating method of fishing

Rogue fishers around the world toss explosives into the sea and scoop up bucketloads of stunned or dead fish, a practice that is illegal in many nations and can destroy coral reefs and wreak havoc on marine biodiversity. Catching perpetrators amid the vastness of the ocean has long proved almost impossible, but researchers working in Malaysia have now adapted acoustic sensors—originally used to locate urban gunfire—to pinpoint these marine blasts within tens of meters.

Growing human populations and international demand for seafood are pushing fishers to increase their catches. "Fish bombing," which is practiced not only in Malaysia but also in Nicaragua, Tanzania and other places, is a "brutally efficient" way to do so, says George Woodman, founder of the Hong Kong-based Teng Hoi Conservation Organization. Shock waves from the explosions rupture the fishes' swim bladders, immobilizing the fish and causing some to float to the surface. And the bombs themselves are easy to make: ammonium nitrate (a common



Coral damage (1) resulting from fish bombs, such as the one depicted (2).

fertilizer) and diesel fuel are mixed in an empty bottle and topped with a detonator and waterproof fuse, Woodman says.

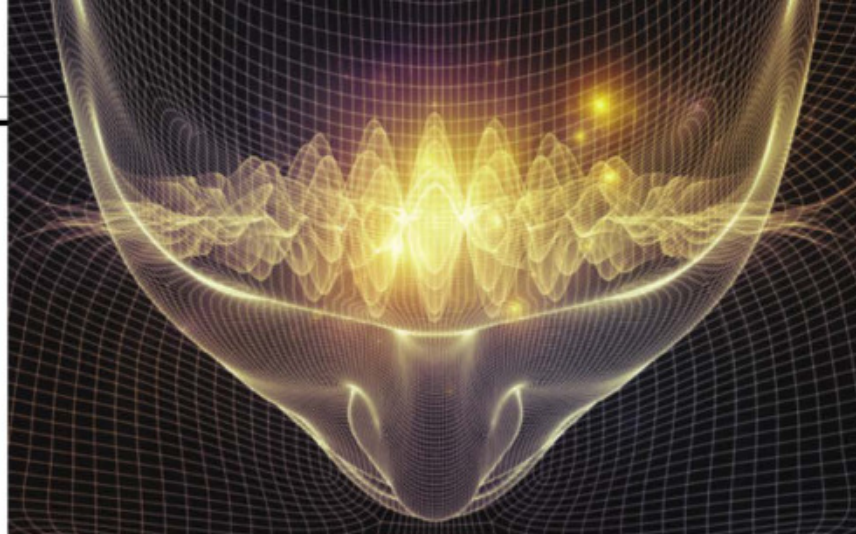
He and his colleagues detonated 19 fish bombs in a part of a bay devoid of marine life in Sabah, a state in East Malaysia. They recorded the explosion sounds with sensors developed by ShotSpotter, a California company that employs similar technology to

home in on gunshots in cities. The team used time-stamped data recorded by four devices mounted on piers and two attached to boats to triangulate the positions of 16 explosions to within 60 meters in about 10 seconds. The researchers also located uncontrolled blasts set off by local fishers and photographed boats in the explosions' vicinity, they reported in March in *Marine Pollution Bulletin*.

These demonstrations—the first time fish bombings have been traced in this way—are an important step toward policing the problem, the team suggests, because an explosion can be linked to a boat in the same location at the same time.

But eradicating fish bombing will take more than just enforcement, cautions Elizabeth Wood, a marine biologist working in Sabah, who was not part of the new study. "It's vital that local fishing communities appreciate the immediate and long-term benefits of sustainable fishing," she says. Malaysian officials are proposing an initiative to promote fish farming, says Ming Yuk Pang, Sabah's assistant minister of tourism, culture and environment and chair of the local Anti-Fish Bombing Committee. "We want to tell them there's a better way to make a living." —Katherine Kornei

BOB HALSTEAD/Getty Images (1); ALAMY (2)



NEUROSCIENCE

Thinking Slow

Super low frequency brain waves are linked to conscious states

Every few seconds a wave of electrical activity travels through the brain, like a large swell moving through the ocean. Scientists first detected these ultraslow undulations decades ago in functional magnetic resonance imaging (fMRI) scans of people and other animals at rest—but the phenomenon was thought to be either electrical “noise” or the sum of much faster brain signals and was largely ignored.

Now a study that measured these “infraslow” (less than 0.1 hertz) brain waves in mice suggests they are a distinct type of brain activity that depends on an animal’s conscious state. But big questions remain about these waves’ origin and function.

An fMRI scan detects changes in blood flow that are assumed to be linked to neural activity. “When you put someone in a scanner, if you just look at the signal when you don’t ask the subject to do anything, it looks pretty noisy,” says Marcus Raichle, a professor of radiology and neurology at Washington University School of Medicine in St. Louis and senior author of the new study, published in April in *Neuron*. “All this resting-state activity brought to the forefront: What is this fMRI signal all about?”

To find out what was going on in the brain, Raichle’s team employed a combination of calcium/hemoglobin imaging, which uses fluorescent molecules to detect the activity of neurons at the cellular level, and electrophysiology, which can record signals from cells in different brain layers.

They performed both measurements in awake and anesthetized mice; the awake mice were resting in tiny hammocks in a dark room.

The team found that infraslow waves traveled through the cortical layers of the awake rodents’ brains—and changed direction when the animals were anesthetized. The researchers say these waves are distinct from so-called delta waves (between 1 and 4 Hz) and other higher-frequency brain activity.

These superslow waves may be critical to how the brain functions, Raichle says. “Think of, say, waves on the water of Puget Sound. You can have very rough days where you have these big groundswells and then have whitecaps sitting on top of them,” he says. These “swells” make it easier for brain areas to become active—for “whitecaps” to form, in other words.

Other researchers praised the study’s general approach but were skeptical that it shows the infraslow waves are totally distinct from other brain activity. “I would caution against jumping to a conclusion that resting-state fMRI is measuring some other property of the brain that’s got nothing to do with the higher-frequency fluctuations between areas of the cortex,” says Elizabeth Hillman, a professor of biomedical engineering at Columbia University’s Zuckerman Institute, who was not involved in the work. Hillman published a study in 2016 finding that resting-state fMRI signals represent neural activity across a range of frequencies, not just low ones.

More studies are needed to tease apart how these different types of brain signals are related. “These kinds of patterns are very new,” Hillman notes. “We haven’t got much of a clue what they are, and figuring out what they are is really, really difficult.”

—Tanya Lewis



Big Sur



Yosemite

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SPACE

The Power of Science Museums

The new air and space museum director talks about the next generation of explorers and the post-truth era

Ellen Stofan, NASA's former chief scientist, recently became the first woman to lead the Smithsonian Institution's National Air and Space Museum. At NASA, Stofan supported commercial activity in low-Earth orbit, helped to develop a long-term plan to send humans to Mars and gave talks at schools around the world to encourage children—especially those in underrepresented groups—to pursue science careers. At the museum, she plans to further that commitment by overseeing a sweeping, multiyear upgrade meant to improve the experience for all of the museum's seven to eight million annual guests. Shortly before starting her new job, Stofan spoke with *Scientific American* about the power of museums to influence the next generation of scientists and to reverse attacks on science. An edited excerpt of that conversation follows.

—Shannon Hall

Scientific American: *How did the museum influence you as a child and in your early career?*

Ellen Stofan: It was just this awe-inspiring place. There's a difference between hearing the stories of the Wright brothers and looking at the Wright Flyer airplane in front of you or seeing an Apollo capsule and rubbing a moon rock. Then, after my sophomore year in college, I had an internship at the museum, where I did whatever needed to be done as the low-level intern coming in for the summer. And I loved it. To me, it was the biggest thrill in the world to walk through those doors in the morning before the museum opened and just look around that place and think, "This is magical. It can't get any better than this."

How does it feel to be the museum's director and the first woman leader?

It's daunting. It's intimidating. I feel incred-



"Are we doing the best possible job we can to inspire that next generation of explorers?"

—Ellen Stofan, National Air and Space Museum

ibly honored to lead the museum, and I'm incredibly excited.

If you could accomplish one goal in your new job, what would it be?

I'm always asking, "Are we doing the best possible job we can to inspire that next generation of explorers?" I want to make sure we're telling the stories that haven't been highlighted before, like what we've seen in the past few years with the book and film *Hidden Figures*, about the African-American women who supported the space program. No matter what child comes into the museum, they should see themselves in those accomplishments. To me, that's what helps to inspire the next generation. I want them not only to look at the amazing time period we're walking into but to ask, "How can I be part of this?"

Why do you think the museum is so popular?

I think that space and aviation—pushing

the boundaries, getting off the surface of Earth, up into the sky and then out into space—inspire all kids and the kid in all of us. I believe that's what drives people to the museum—that wow factor: "Wow, what great things we can accomplish when we put our minds to it."

Can museums like yours help to combat the so-called post-truth era?

I hope so. I think a lot of people honestly are confused. They don't know where information is coming from. But we are a museum that says, "Look, we can lay out for you step by step where this information comes from and how our scientists use this information to better understand not just our planet but all the planets of the solar system and worlds beyond our solar system." We can help people put science, the scientific process and fact-based thinking into practice.

IN THE NEWS

Quick Hits

U.S.

Hawaii's state legislature announced it wants to get 100 percent of its energy from renewable sources by 2045. The state already gets more than a quarter of its electricity from such sources.

PACIFIC OCEAN

A whale shark set a new distance record for its species by swimming more than 20,000 kilometers across the Pacific Ocean in 841 days. The creature, named Anne, traveled from off the western coast of Panama to near the Mariana Trench.

U.K.

Caterpillars of the oak processionary moth invaded London's parks this spring. The creatures' long white hairs can irritate eyes and skin and cause sometimes deadly allergic reactions.

SWEDEN

Archaeologists discovered the remains of a bloody slaughter in a Swedish fort from the fifth century A.D. The 26 skeletons they excavated (including those of an old man and a teenager) show wounds from behind, suggesting a surprise attack.

JAPAN

A Japanese engineer built a giant robot inspired by the animated TV show *Mobile Suit Gundam*, fulfilling a childhood dream. The machine, made by farming machinery company Sakakibara Kikai, stands 8.5 meters tall and weighs more than seven metric tons.

SUDAN

New high-resolution images of a meteorite found in the Nubian Desert in 2008 revealed it contains diamonds—possibly from a “lost” planet that orbited the sun during the solar system's formation, scientists say.

For more details, visit
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—Tanya Lewis

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✓Yes



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✓Yes



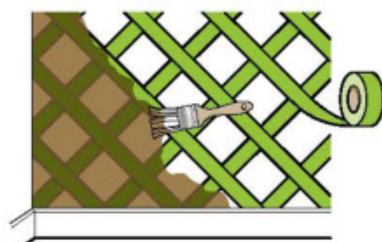
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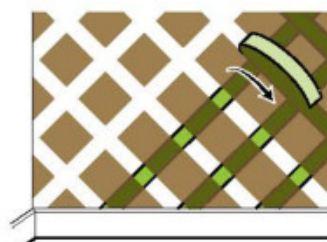
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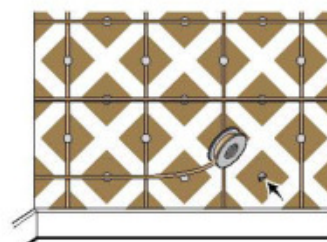
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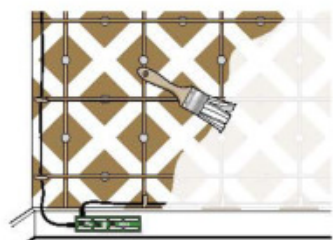
1 First, researchers covered the wall with a lattice of painter's tape and painted over it with nickel paint.



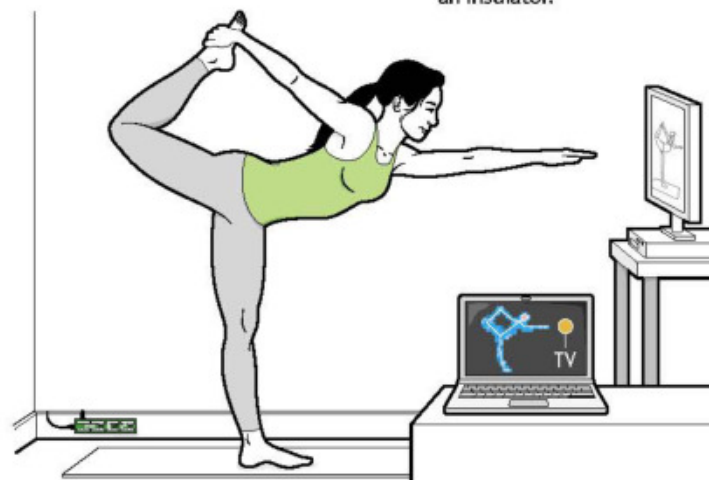
2 Next, they removed the tape, leaving behind a diamond pattern of electrodes.



3 They connected the diamonds using thin copper tape, with a circular vinyl sticker in the middle of each electrode as an insulator.



4 They wired the copper tape to a circuit board plugged into the wall and covered the wall with regular latex paint.



5 The wall was then ready to track gestures and detect nearby appliances.

TECH

Smart Walls

Special paint turns a surface into a giant touch sensor

The right paint can add pizzazz to your walls—and now it can also make them smarter. Researchers recently converted a wall into an outsize trackpad and motion sensor by using low-cost conductive paint to create a large grid of electrodes.

Such a smart wall can sense human touch and track gestures from a short distance. It can also detect the locations of appliances and whether they are switched on. The technology could someday turn on lights when a person enters a room, track a player's motion in an interactive video game or monitor a child's television use. "Walls are everywhere, so why not turn them into sensors for smart homes?" says Yang Zhang, a computer science doctoral student at Carnegie Mellon Univer-

sity, who helped to develop the concept.

To create the high-tech surface, Zhang and his colleagues applied painter's tape in a lattice pattern to a 12-by-eight-foot wall, then coated it with commercially available conductive nickel paint. Removing the tape left a pattern of diamond-shaped electrodes, which the researchers connected using a grid of thin copper tape strips. They affixed a vinyl sticker in the middle of each diamond to insulate the electrodes from one another. Finally, they wired the strips to a custom-built circuit board and covered the wall with standard latex paint. The entire project took four hours and cost less than \$200. In theory, Zhang says, "anyone can use the technique to make a wall smart."

In tracking a touch or gesture, the wall functions similarly to a smartphone screen. The circuit board prompts the electrodes to emit an electric field; when a person's body intercepts this field, it triggers a measurable change in current at the nearby electrodes. The user must be within three feet of the

wall for it to work, however—a limitation the researchers are working to overcome.

In the wall's appliance-detection mode, the power is turned off, and the electrodes act as an antenna to passively pick up electromagnetic waves emitted by nearby devices. The researchers detected iPads up to 6.5 feet away from the wall; fans and floor lamps could be sensed from about 10 feet. Zhang and his colleagues at Disney Research presented the wall in April at the CHI Conference on Human Factors in Computing Systems in Montreal.

Engineers have long dreamed of technologies that blend into our surroundings, says Christian Holz, a research scientist at Microsoft Research in Redmond, Wash., who was not involved in the work. A wall sensor is pervasive yet hides in plain sight, he notes: "It nicely questions our understanding of what a device might be and demonstrates how rich sensing technology can seamlessly integrate with everyday objects." —Prachi Patel

SOURCE: "WALL++: ROOM-SCALE INTERACTIVE AND CONTEXT-AWARE SENSING," BY YANG ZHANG ET AL., PRESENTED AT CHI CONFERENCE ON HUMAN FACTORS IN COMPUTING SYSTEMS, MONTREAL, APRIL 21-26

EVOLUTION

Blue's Clues

Wealthy families invest more in boys, backpack sales suggest

Parents tend to favor children of one gender in certain situations—or so evolutionary biologists tell us. A new study used colored backpack sales data to show that parental wealth may influence spending on sons versus daughters.

In 1973 biologist Robert Trivers and computer scientist Dan Willard published a paper suggesting that parents invest more resources, such as food and effort, in male offspring when times are good, and in female offspring when times are bad. According to the Trivers-Willard hypothesis, a son given lots of resources can outcompete others for mates—but parents with few resources are more inclined to invest them in daughters, who generally find it easier to attract reproductive partners. Trivers and Willard further posited that parental circumstances could



even influence birth ratios, a concept widely supported by research across species.

Studying parental investment *after* birth is difficult, however. The new study looked for a metric of such investment that met several criteria: it should be immune to inherent sex differences in the need for resources; it should measure investment rather than outcomes; and it should be objective.

Study author Shige Song, a social demographer at Queens College, City University of New York, examined spending on pink and blue backpacks purchased in China in 2015 from a large retailer, JD.com. He narrowed the data to about 5,000 bags: blue backpacks bought by households known to

have at least one boy and pink ones bought by households known to have at least one girl. The results showed that wealthier families spent more on blue versus pink backpacks—suggesting greater investment in sons. Poorer families spent more on pink packs than blue ones. The findings were published online in February in *Evolution and Human Behavior*.

Song's evidence for the Trivers-Willard hypothesis is "indirect" but "pretty convincing," says Rosemary Hopcroft, a sociologist at the University of North Carolina at Charlotte, who was not involved in the new study. Hopcroft reported in 2016 that U.S. fathers with prestigious occupations were more likely to send their sons to private school than their daughters, whereas fathers with lower-status jobs more often enrolled their female children. Although the new study does not prove the families were buying the blue backpacks for boys and pink ones for girls, Hopcroft notes that "it's a clever and interesting paper, and it's a very novel use of big data."

—Matthew Hutson

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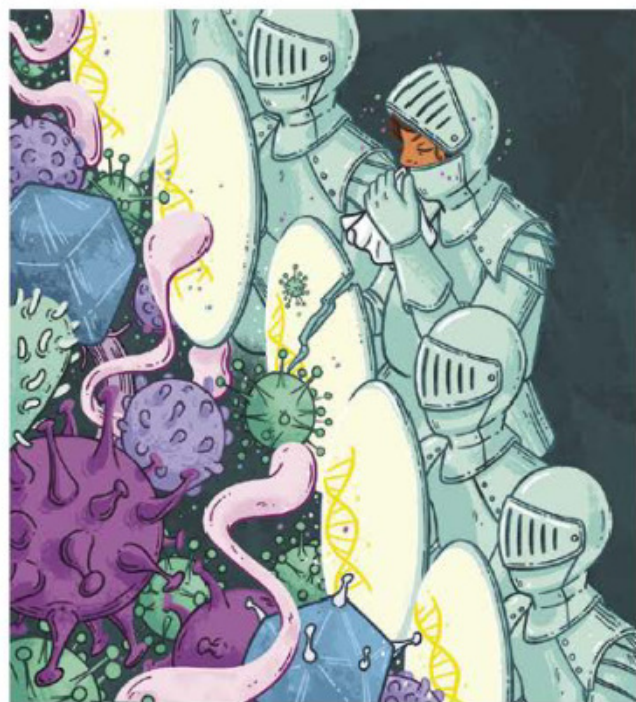
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Claudia Wallis is an award-winning science journalist whose work has appeared in the *New York Times*, *Time*, *Fortune* and the *New Republic*. She was science editor at *Time* and managing editor of *Scientific American Mind*.



Killer Infection: Is It Your Genes?

Subtle mutations can undermine
our ability to fend off a specific bug

By Claudia Wallis

Bad luck. Terrible misfortune. That's what we think when we hear about a perfectly healthy child who suddenly dies of influenza, a virus most of us can shake off. But what if it isn't luck? What if this kind of deadly infection turns out to be, well, genetic?

Crazy as that sounds, there is a growing body of research that supports the idea. Much of it has been led by Jean-Laurent Casanova, a pediatric immunologist and geneticist at the Rockefeller University. Casanova wanted to unravel those tragic cases of flu, in which a child with no apparent underlying illness wound up in the intensive care unit. He was equally intrigued by other infections that are perfectly survivable or even innocuous for most of us but send some individuals to their grave.

There are many examples of what Casanova calls "the infection enigma." Herpes simplex viruses, for instance, can cause annoying cold sores and genital lesions in many people, but in rare cases they invade the brain and incite potentially lethal encephalitis. *Candida albicans* is a ubiquitous fungus that typically causes serious harm only to people with a weakened immune system, and yet some otherwise healthy individuals suffer repeated bouts of infection. Even with a dire disease such as tuberculosis, Casanova

notes, in places where the TB bacterium is endemic, "everyone inhales it, but not everyone gets sick and fewer than one in 100 will die of TB." This can't just be the fickle finger of fate, he reasoned.

In some cases, susceptibility to a specific kind of infection—*Candida*, for example—runs in families. This was Casanova's big clue. He hypothesized that some of us harbor genetic mutations, whether inherited or spontaneous, that make us susceptible to a particular germ, much the way certain strains of wheat are genetically vulnerable to a particular blight.

Over the past two decades Casanova, often working with Laurent Abel of Necker Hospital for Sick Children in Paris, and a few other laboratories have identified dozens of **single-gene mutations causing this kind of vulnerability**. These mutations do not devastate defenses, as with severe combined immunodeficiency (SCID), once known as "bubble boy" syndrome and now treated with bone marrow transplants. Instead, Casanova explains, "these are pathogen-specific diseases caused by inborn errors of immunity that are very narrow—sometimes [involving] one virus, one bacterium."

In the case of severe flu, Casanova's team has identified two gene defects, **one that limits the production of virus-fighting interferons** and one not yet published. With herpes simplex encephalitis, one category of mutations lays carriers open to infection in the front of the brain. **A second type causes vulnerability to encephalitis in the hindbrain.** With flu, children eventually develop antibody protection that compensates for the genetic flaw; the same is likely true for herpes. Most of these mutations are rare, but Casanova says his lab recently found a defect that causes vulnerability to TB and is present in one in 600 people of European ancestry and one in 1,000 humans.

Taken together, these surprising discoveries are creating a paradigm shift in how we think about severe infection. "This work makes the case that we should shift a little of our attention from the germ to the host, or child," says Isabelle Meyts, a pediatric immunologist at University Hospitals Leuven in Belgium. The findings also expand our understanding of the human immune system, especially defenses that do not depend on white blood cells, notes immunologist Helen Su of the National Institute of Allergy and Infectious Diseases. There is great redundancy built into our germ-fighting systems, so it is shocking to learn that initial protection from a specific bug can depend on a single gene.

This research suggests that doctors should do genetic work-ups in puzzling cases of serious infection, Meyts says. The results can sometimes guide treatment. For example, Casanova and others have found more than a dozen mutations that disrupt the body's ability to battle non-TB mycobacteria, and all of them mess with interferon gamma—a key immune system activator. Giving such patients this interferon "works beautifully," Casanova says. "It's like insulin for diabetic patients."

A genetic analysis could also enable doctors to counsel relatives on who else is at risk. Crucially, families can come to understand that a loved one died of infection because of a flawed gene. "The fact that they have an answer is a tremendous solace," Su observes. Or as Casanova puts it: "It's not that they had too much McDonald's; it's not pollution." And it's not just bad luck. ■

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The Next Round of Merger Mania

12 ideas for new companies that probably won't exist—but should

By David Pogue

These days—have you noticed?—it's not enough for companies in the digital economy to become behemoths astride the world. They've begun growing tentacles into *each other*. The idea is to combine complementary perks of two companies, adding value to your subscriptions. Making it less likely you'll choose a competitor.

That's why T-Mobile recently partnered with Netflix (T-Mobile subscribers get a free Netflix subscription), Netflix partnered with Comcast (you pay for Netflix as part of your Comcast bill), Amazon partnered with Best Buy to develop television sets (if you buy your TV at Best Buy, you get Amazon Fire technology built in), and Chevrolet partnered with Shell (you pay for gas at Shell stations with a few taps on your dashboard screen).

All good, right? Who doesn't like greater convenience and more free services?

Of course, there could be a darker side to this kind of conglomeration, too: many companies already collect insane amounts of data about you and your behavior, and the bigger the company, the more data it'll have.



David Pogue is the anchor columnist for Yahoo Tech and host of several NOVA miniseries on PBS.

But never mind all that. Merge-o-mania is under way, and nothing's going to stop it. We may as well get used to it. In fact, we may as well have some fun with it—by imagining some future ventures that at least hold some entertainment value.

Surely, it won't be long before we are reading about joint enterprises like these:

- Uber and Tinder team up to form Tunder. Swipe right if you see someone who's appealing enough to go for a drive with you!
- Ticket reseller StubHub and restaurant delivery service GrubHub finally enjoy their inevitable pairing. They bring you StubGrub: the digital marketplace for reselling takeout meals you ordered by mistake.
- Millions of people have used the free app Duolingo to gain skills in a new language; Fandango is the ultimate movie showtimes guide. Together these fine companies bring you Fandango, the app for foreign-language films that explains what the heck is going on.
- Fitbit and Twitter are natural partners for creating FitBitter. Yes, now there's a discussion network just for people who channel their frustrations in life into obsessive workouts.
- It's Sirius XM Radio meets Apple's Siri voice-control assistant! Now you can subscribe to Siri XM, which misunderstands your spoken requests for more than 500 channels of sound.
- Crafter marketplace Etsy and Netflix join forces to bring you Netsyflix. For the first time, you can binge-watch season-long episodes of people crocheting smartphone cases.
- Subway and Grindr offer GrindrGrindr, the app that lets you meet an attractive partner for sharing a hero sandwich.
- From the makers of Spotify and Lyft, it's Spyft! With one tap, you can summon a driver who's put together a huge number of awesome playlists.
- YouTube and Uber find common ground in their new offering, YuberTube. Open the app and tap "Confirm Location"—and within minutes, a driver comes to *you* with a selection of music videos and adorable cat footage.
- What could be hotter than a collaboration between Tesla and Instagram? Meet TeslaGram: the premiere network for selfies of people posing with cars they can't afford.
- Amazon's Alexa voice assistant gets smarter every year. And Yelp's crowdsourced database of restaurant and other reviews continues to flourish. It's time, then, for Ayelpa, the home assistant that listens in as you gripe about the lousy meal you just had and automatically posts your complaint online to warn others.
- AT&T and Snapchat's new venture is called SnapchATT. Now middle schoolers will have an easy way to make really short phone calls that they instantly forget.

Okay, okay. In the real world, most of these ideas will never come to pass. But we can always dream, can't we? 

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MERGER IDEAS MY TWITTER FOLLOWERS HAVE DREAMED UP:
scientificamerican.com/jul2018/pogue

The Agenda Setters

Bringing Science to Life

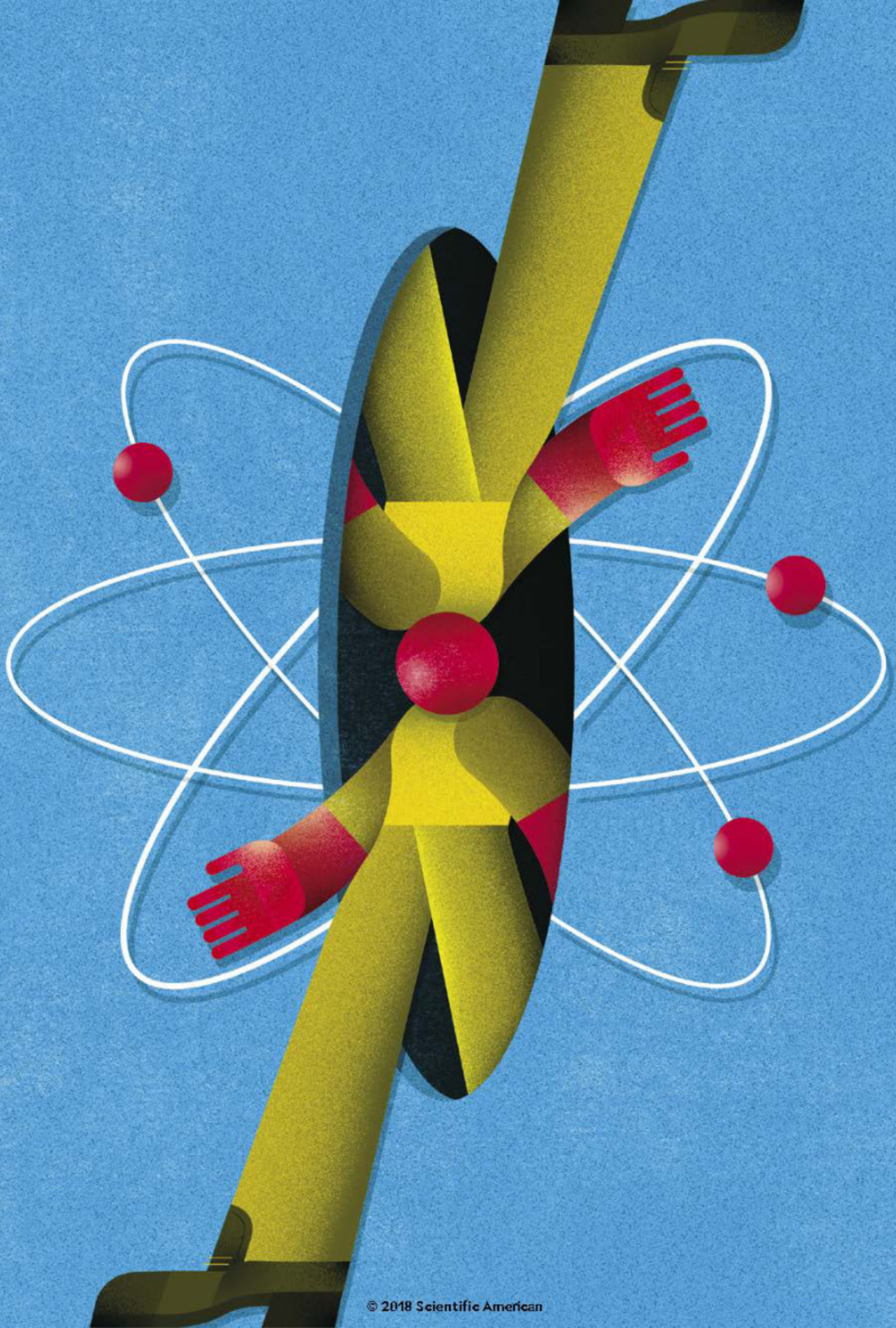


A Conversation on Harmonizing the Nomenclature for Biologic Medicines

The Source | Washington, DC | April 11th, 2018

Scientific American's Custom Media Division in partnership with the Alliance for Safe Biologic Medicines convened a luncheon conversation in Washington, DC to discuss issues surrounding the viability of biologic/biosimilar naming with an overarching goal of aligning on a global approach for naming harmonization. The forum provided an opportunity for regulators to hear from key stakeholders (patients, advocacy groups, physicians, pharmacists) as to their opinions on biologic naming.

The discussion was moderated by **Brady Huggett**, Business Editor of Nature Biotechnology and included representatives from the following organizations: **Doug Badger**, Alliance for Safe Biologic Medicines; **Madelaine Feldman**, MD, FACR, Alliance for Safe Biologic Medicines; **Joe Franklin**, JD, PhD, U.S. Food and Drug Administration; **Harry Gewanter**, MD, FAAP, FACR, MACR Rheumatologist; **Anna Hyde**, Arthritis Foundation; **Jeff Jones**, PhD, SoCal Bioinformatics; **Edward Li**, MD, Hematology/Oncology Pharmacy Association (HOPA); **Lubna Merchant**, MS, PharmD, U.S. Food and Drug Administration; **Vincent Pacileo**, Arthritis Foundation; **Natasha Pattanshetti**, JD, MPH, American Academy of Dermatology Association; **Peter Pitts**, Center for Medicine in the Public Interest; **Michael Reilly**, Esq., Alliance for Safe Biologic Medicines; **Dawn Richards**, Canadian Arthritis Patient Alliance; **Anthony Ridgway**, Centre for Evaluation of Radiopharmaceuticals & Biotherapeutics, BGTD at Health Canada; **Michael Roberts**, American Gastroenterological Association; **Phillip Schneider**, MS, FASHP, FASPEN, Alliance for Safe Biologic Medicines; **Andy Spiegel**, Global Colon Cancer Association; **Sadie Whittaker**, Alliance for Safe Biologic Medicines.



PHYSICS

CROSSING THE QUANTUM DIVIDE

The universe according to quantum mechanics is strange and probabilistic, but our everyday reality seems nailed down. New experiments aim to probe where—and why—one realm passes into the other

By Tim Folger

Illustration by Maria Corte

Tim Folger is a freelance journalist who writes for *National Geographic*, *Discover* and other national publications. He is also the series editor for *The Best American Science and Nature Writing*, an annual anthology published by Houghton Mifflin Harcourt.



MOST OF SIMON GRÖBLACHER'S HANDIWORK IS INVISIBLE TO THE NAKED EYE. One of the mechanical devices he fashioned in his laboratory at Delft University of Technology in the Netherlands is just a few millionths of a meter long—not much bigger than a bacterium—and 250 nanometers thick—about a thousandth of the thickness of a sheet of paper. Gröblacher no doubt could continue to shrink his designs, but he has a different goal: he wants to scale things *up*, not down. “What we’re trying to do is make things that are really, really big,” he says as he brings up images of hardware on his computer. Keep in mind that for Gröblacher, an experimental physicist, “really, really big” means something just barely visible without a microscope, “a millimeter by a millimeter in size.”

IN BRIEF

The microscopic and macroscopic worlds do not blend seamlessly: the probabilistic nature of quantum mechanics reigns over the first, whereas the second observes more logical “classical” rules.

Physicists have long been stymied over the question of where one realm ends and the other begins, but upcoming experiments offer hope of testing different theories.

One possibility, called continuous spontaneous localization, suggests that quantum probabilities randomly collapse into classical certainties. If true, these collapses would also create a sea of background vibrations in the universe that experiments could detect.

By working on that less than humongous scale, Gröblacher hopes to address an extraordinary question: Can a single macroscopic object be in two places at once? Could something the size of a pinhead, say, exist both here and there at the same time? That seemingly impossible condition is actually the norm for atoms, photons and all other particles. According to the surreal laws of quantum theory, reality at its most basic level defies our commonsense assumptions: Particles do not have fixed positions, energies or any other definite properties—at least while no one is looking. They exist in numerous states simultaneously.

But for reasons physicists do not understand, the reality we see is different. Our world—even the parts we cannot observe directly—appears to be distinctly *unquantum*. Really big things—meaning anything from a virus on up—always manifest in one place and one place only; there is just one Gröblacher talking to one jet-lagged, scribbling journalist in his Delft lab. And therein lies a mystery: Why, if everything is built on a quantum blur of matter and energy, do we not experience quantum weirdness ourselves? Where does the quantum world end and the so-called classical world of Newtonian physics begin? Is there a rift in reality, a scale beyond which quantum effects simply cease? Or does quantum mechanics reign everywhere, and we are somehow blind to it?

“We know the microworld is quantum, and we know in one way or another, we are classical—what-

ever that means,” says Angelo Bassi, a theoretical physicist at the University of Trieste in Italy. “We are ignorant about the true nature of matter in between the micro and the macro.” That no-man’s-land has baffled physicists since the birth of quantum theory a century ago. But in recent years Gröblacher and other physicists have started running exquisitely sensitive tabletop experiments that may one day reveal how objects make the startling transition from quantum to quotidian. Whether those efforts will resolve the mysteries of quantum theory or deepen them, no one can yet say. But in probing the wild and woolly quantum borderlands, researchers stand a chance of discovering a whole new realm of physics.

THE MEASUREMENT PROBLEM

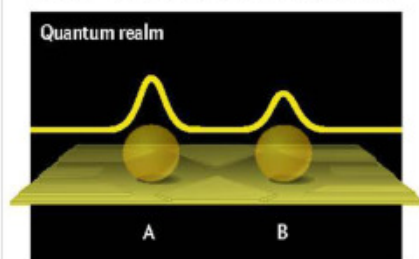
FOR ALL ITS PARADOXES, quantum mechanics is the most powerful and exacting scientific theory ever devised. The theory’s predictions match experiment with ridiculous precision—to better than parts-per-trillion accuracy in some cases. By revolutionizing our understanding of atomic structure, it transformed every facet of science, from biology to astrophysics. Without quantum theory, there would be no electronics industry, no cell phones, no Google. Yet the theory has one glaring shortcoming, says Stephen L. Adler, a theoretical physicist at the Institute for Advanced Study in Princeton, N.J.: “In quantum mechanics, things don’t happen.”

Separate Realms

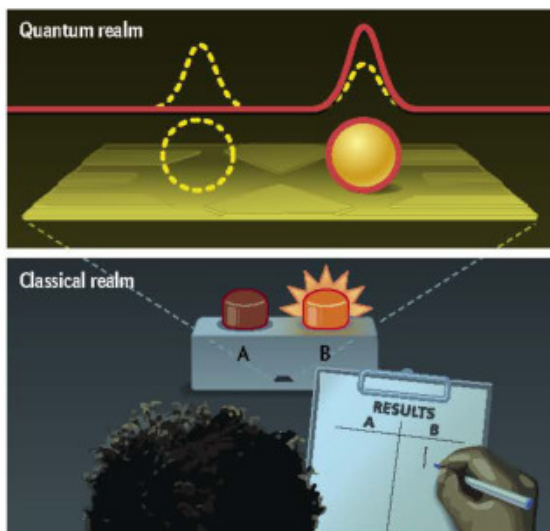
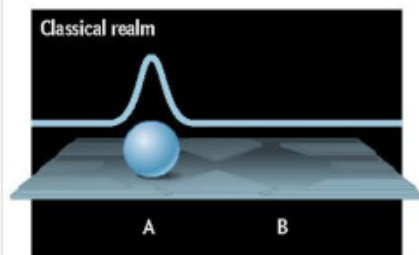
Quantum mechanics produces some bizarre effects in the microscopic world, but we do not see these phenomena in our macroscopic, “classical” reality. Why is that? Scientists have never understood why and how the universe crosses over between these realms, but several theories, as depicted here, offer possible explanations.

Quantum vs. Classical

According to quantum mechanics, particles do not exist in definite states—here or there, having this energy or that—but rather take on all possible states and positions. The theory describes particles with equations called wave functions, which are combinations, or “superpositions,” of multiple waves. The amplitude of each peak in a wave function denotes the probability of a particle being found in any specific circumstances—for instance, at point A or B, as shown.

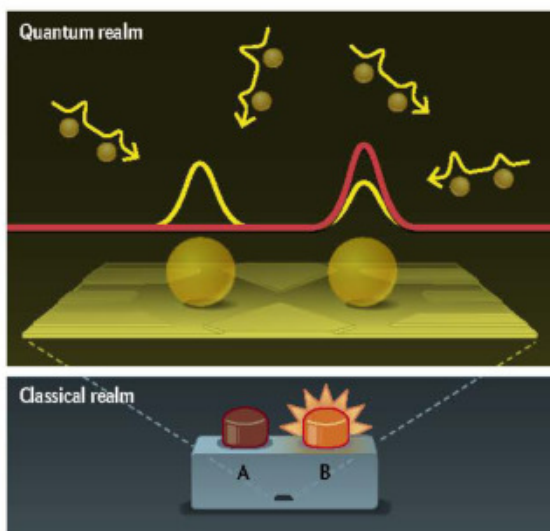


Strangely, when scientists make a measurement of a particle, this act appears to reduce all the quantum possibilities to one, seemingly chosen at random. The experiment will find the particle at point A, for example, and the particle enters the classical realm, ceasing to be in a superposition.



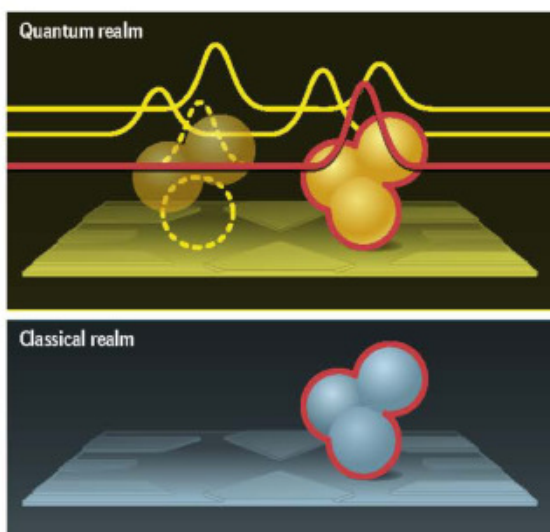
Collapse at Measurement

One theory for how the universe crosses over from quantum to classical is that the act of measurement intervenes. Particles can linger in quantum superpositions (dotted yellow lines) as long as no one looks too closely, but once humans make a measurement, the particle is forced to “choose” a specific state (solid red lines). How this happens, and why human measurement should take on such a significance in physics, remains mystifying.



Decoherence

Another theory posits that a particle's environment is to blame for moving it from the quantum world to the classical. As long as a particle is undisturbed by any outside influence, so the thinking goes, it can remain in superposition. But when the wave functions of other particles or objects nearby meet with its own, they interfere, causing the particle's many quantum possibilities to collapse into a single classical reality.



Continuous Spontaneous Localization

Another possibility is that the collapse of the wave function to a single possibility is a random event, not caused by human or environmental interference. The chances of any one particle collapsing at any given time are extremely small, but in macroscopic objects containing multitudes of atoms, the collapse of at least one is inevitable, which then causes the entire structure to collapse.

Adler's cryptic comment refers to what the basic equations of quantum theory say—or do not say—about the nature of reality. Known as wave functions, the equations assign probabilities to an object's chances of being found in various states. Unlike Newtonian physics, where apples, planets and everything else always have well-defined properties, quantum physics is inherently probabilistic. In a sense, particles that are described by wave functions cannot even be said to fully exist; they have no fixed locations, speeds or energies—only probabilities. But everything changes when scientists take a measurement. Then real, tangible properties arise, as if conjured up by merely attempting to observe them. Not only does the theory not say *why* measurements bring about this transformation—it does not tell us why one of those many possibilities manifests instead of others. Quantum mechanics describes what *might* happen as the outcome of a measurement but not what *will* happen. In other words, the theory provides no mechanism for the transition from the probable to the actual.

To “make things happen” in quantum mechanics, one of the theory's legendary founders argued for an almost metaphysical hack. In the late 1920s Werner Heisenberg formulated and spread the notion that the very act of measurement makes the wave function of a particle “collapse”—the many potential outcomes instantaneously reduce to a single observed result. The only flaw with the idea is that there is nothing in the equations of quantum theory that says a collapse occurs or offers a physical process to explain it. Heisenberg's “solution” essentially introduced a new mystery into physics: What exactly happens when a wave function collapses? That quantum conundrum is now known as the measurement problem.

Physicists may have gotten used to the collapse idea over the past 90 years, but they have never really liked it. The notion that a human action—measurement—plays a central role in our most fundamental theory of how the universe works does not sit well with anyone partial to the concept of an objective reality.

“Fundamentally, I have an ideal of what a physical theory should be,” says Nobel laureate physicist Steven Weinberg of the University of Texas at Austin. (Weinberg serves on *Scientific American's* board of advisers.) “It should be something that doesn't refer in any specific way to human beings. It should be something from which everything else—including anything you can say systematically about chemistry, or biology, or human affairs—can be derived. It shouldn't have human beings at the beginning in the laws of nature. And yet I don't see any way of formulating quantum mechanics without an interpretive postulate that refers to what happens when people choose to measure one thing or another thing.”

CHOOSE YOUR INTERPRETATION

ONE SLEIGHT-OF-HAND WAY OUT of the measurement problem is to assume that collapse simply does not happen. In the early 1970s H. Dieter Zeh, now an emeritus professor at the University of Heidelberg in Germany, proposed a process that yields the *appearance* of collapse while preserving the full quantum multiplicity of the wave function. In the real world, Zeh argued, the wave function of any particular object becomes hopelessly enmeshed with that of everything else in its environment, making it impossible to keep track of all the countless quantum interactions going on around us. In quantum parlance, the wave functions become “entangled”—a special kind of correlation that preserves connectedness even over huge distances. An observer can only ever hope to look at a single small part of that vast entangled system, so any particular measurement captures just a sliver of the quantum world.

Zeh called this process “decoherence,” and it has become the go-to explanation among physicists for why we do not witness quantum phenomena on a macroscopic level. It describes how an intact wave function—which comprises all the possible physical states a particle might have—decoheres as it mingles with the wave functions of other quantum systems around it. If the decoherence model is right, we ourselves live among the strands of that entangled quantum web but see only part of it.

Not all physicists believe that decoherence settles the measurement problem. For one thing, it still fails to explain why we see one strand of the quantum web and not others. “You still have to invoke the collapse postulate, which takes an entangled state and says that one of those possible states has to be selected, and that is usually done by fiat,” says Miles P. Blencowe, a theoretical physicist at Dartmouth College. For Blencowe and others, the process does not capture the way we experience things. “I believe we have this one world that is evolving,” he says. “How do you go from an entangled state to this perception of the world as always finding one unique path into the future? Many quantum mechanicians would feel that there needs to be a collapse to restore this oneness about the world as it evolves rather than this web of entanglement that keeps enlarging.” Adler's assessment of decoherence is more blunt: “It doesn't supply a mechanism [for collapse] at all. It doesn't solve the problem, period.”

Six decades ago a doctoral candidate at Princeton University proposed an even more radical solution to the collapse problem. In his 1957 Ph.D. thesis, Hugh Everett argued that the wave function neither collapses nor decoheres. Rather all its components are physically real, parts of an endlessly branching panoply of universes. Everett's “many worlds” interpretation, as it is called, has become popular among cosmologists, who have other reasons to think we might inhabit a multiverse. But no one has ever

managed to experimentally distinguish the many-worlds idea from standard quantum theory.

The same holds for other interpretations of quantum mechanics. French physicist Louis de Broglie, one of the founders of quantum theory, sought to eliminate the need for collapse by introducing the notion of “pilot waves” that guide the paths of electrons and all other particles. In de Broglie’s version of quantum theory, which American physicist David Bohm further developed in the 1950s, there is no mysterious collapse; measurements simply show the interactions of pilot waves and their associated particles. But again, no one has yet found experimental evidence that distinguishes de Broglie and Bohm’s pilot-wave view of reality from Everett’s many worlds or any of the other dozen or so different takes on quantum mechanics. In the end, quantum partisans choose their favorite description of reality based on aesthetics. “I still come back to the fact that we have this one world that is evolving,” Blencowe says. “For that, one really needs some sort of collapse, which is more than just a rule for the results of experiments but is some actual process.”

TESTING COLLAPSE

THE CITY OF DELFT might qualify as an entangled quantum system. Its placid canals and medieval brick buildings overlap in space and time with cars, bicyclists, cell-phone shops and students staggering home from all-night parties along the same narrow streets painter Johannes Vermeer once walked. Gröblacher’s lab lies about two kilometers south of the old town center and what feels like several hundred years into the future. On a warm spring morning, he shows a visitor one of the “really, really big” things he and his colleagues have built: a millimeter-size membrane tethered to a silicon chip, just barely visible to the naked eye.

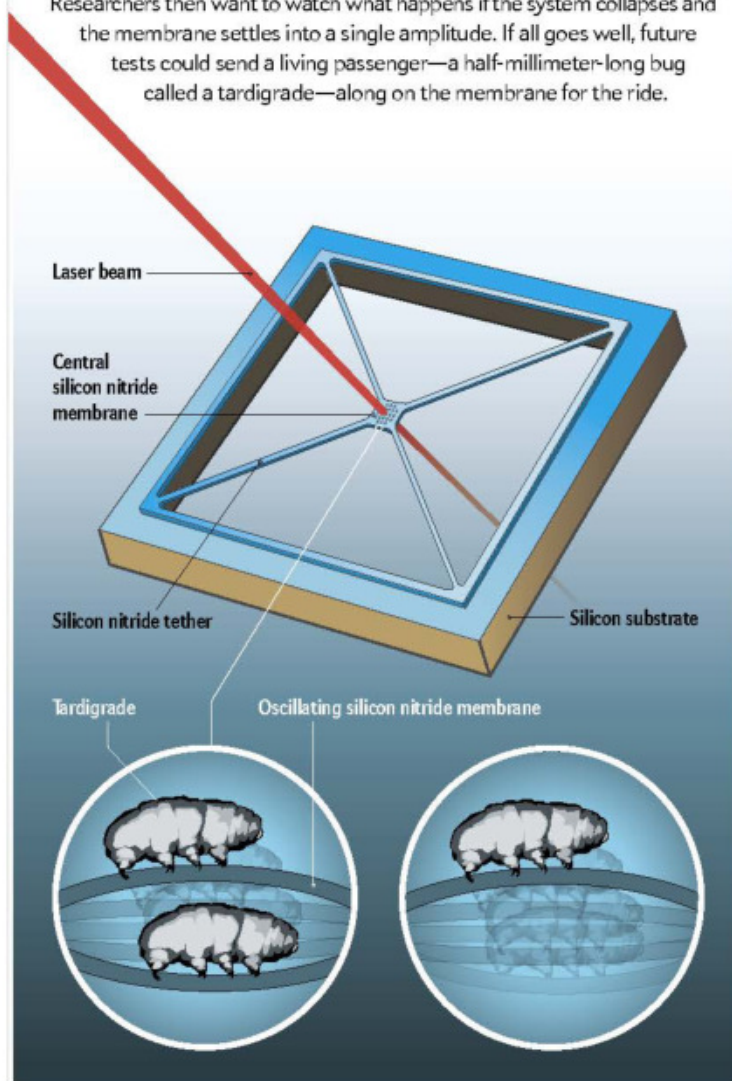
Seen up close (or blown up on a poster in the hallway outside Gröblacher’s office), the membrane resembles a minuscule trampoline. It is made of silicon nitride, a durable ceramic material that was used for engine bearings in the space shuttles, and holds a highly reflective mirror at its center. A single jolt from a component on the chip can set the membrane vibrating for minutes at a time. Such membranes are “really good oscillators,” Gröblacher says. “To put that in perspective, it would be like pushing someone on a swing, and the person would go back and forth, with one single push, for 10 years.” Despite its Lilliputian dimensions, the membrane is extraordinarily robust. “We really put a lot of stress in it—six gigapascals” says Richard Norte, one of Gröblacher’s collaborators. “It’s about 10,000 times the stress you’d have in a bicycle tire, in something that’s only about eight times thicker than the width of DNA.”

Those robust qualities make the membrane an ideal place to study quantum phenomena—it vibrates reliably at room temperature without break-

Tabletop Test

Physicists want to see if macroscopic objects can behave in quantum ways. One planned experiment will feature a millimeter-size membrane that looks like a tiny trampoline. Attached to a silicon chip, the membrane can be jolted into long-lasting vibrations. Ultimately scientists plan to use a laser to push the membrane into a quantum superposition. In the experiment, the membrane could be vibrating at two different amplitudes at once.

Researchers then want to watch what happens if the system collapses and the membrane settles into a single amplitude. If all goes well, future tests could send a living passenger—a half-millimeter-long bug called a tardigrade—along on the membrane for the ride.



ing down. Gröblacher and Norte plan to eventually use a laser to nudge the membrane into a superposition—a quantum state where the membrane could be simultaneously oscillating at two different amplitudes. The membrane’s ability to wiggle for minutes on end should, in principle, allow such quantum states to persist long enough to see what happens when—or if—the membrane collapses into a single classical state.

“That is exactly what you need to create some sort

of quantumness,” Gröblacher says. “You don’t want to have it interact with its environment, because that induces decoherence—supposedly. So you want a really well-isolated system, get it in a quantum state, then switch on your own decoherence, something you control—a laser. We’re still not at the point where we can actually create a superposition of the oscillations of the system. But in a few years that’s what we’re aiming for.”

And Gröblacher and his colleagues do not plan to stop there. The researchers hope to ultimately place a living creature on the membrane and then put the membrane, and any passengers on it, into a quantum superposition. Leading candidates for that mission into quantum space are eight-legged microorganisms called tardigrades, also known as water bears. “They’re amazing creatures,” Gröblacher says. “You can cool them down—they’re still alive; you can heat them up—they’re still alive; put them in a vacuum—they’re still alive.” He admits this step is a bit of a ways off. “It’s not crazy. It’s nice as a long-term goal, but first we have to get our devices into superposition, then we can think about putting in a living organism.”

CONTINUOUS SPONTANEOUS LOCALIZATION

WITH OR WITHOUT TARDIGRADES, such an experiment would allow physicists to test whether nature somehow censors quantum effects above a certain size scale. Some physicists have proposed that collapse might be an actual physical phenomenon, with measurable effects. One idea—known as continuous spontaneous localization, or CSL—is that wave function collapse is simply a random event occurring constantly in the microscopic world. According to CSL, the chance that any one particle will collapse is extremely rare—it might happen once in hundreds of millions of years—but for large aggregates of particles, collapse becomes a certainty.

“A single proton has to wait about 10^{16} seconds to see a collapse, so it happens only a few times over the age of the universe,” Bassi says. But the huge number of particles in any macroscopic object makes collapse inevitable. “If you take a table, which contains roughly Avogadro’s number of particles— 10^{24} —the collapse occurs almost immediately.” If CSL is real, measurement and observation have no role in collapse. In any measurement, a given particle and the devices recording it become part of an immense quantum array that very rapidly collapses. Although it seems as if the particle went from a superposition to an actual position during a measurement, this transformation happened as soon as the particle interacted with the devices, before the measurement occurred.

If collapse turns out to be a real physical phenomenon, the practical consequences could be significant. For one thing, it might limit the nascent technology of quantum computers. “Ideally, you would like to make bigger and bigger quantum computers,” Bassi says. “But you would not be able to run quantum algorithms,



MIRRORS at LIGO showed no evidence of having been nudged by quantum jiggles predicted by CSL theory.

because the collapse would kill everything.” For decades most physicists have regarded collapse as an essentially untestable aspect of quantum theory. But CSL and other collapse models have changed that. The CSL model, for example, predicts that the action of collapse imparts a slight jiggle to particles, creating an omnipresent background vibration that might be detectable in experiments. “The collapse [in CSL] is something universal for micro and macro systems,” Bassi says. “Every time there is a collapse, you move the particle a little.” He and other physicists have searched for such evidence in surprising places. They have combed through the calibration data for the Laser Interferometer Gravitational-Wave Observatory (LIGO), an instrument capable of registering motions 10,000 times as small as the width of a proton.

In February 2016 LIGO reported detecting a gravitational wave for the first time. The wave—a ripple in spacetime caused by two distant colliding black holes—stretched and squeezed the space between two mirrors at the experiment’s twin sites in Washington State and Louisiana. This passing wave shifted the positions of LIGO’s mirrors by just four-thousandths the diameter of a proton, in perfect agreement with predictions by Einstein’s general theory of relativity. But Bassi and his colleagues found no evidence in LIGO’s data for any additional motion caused by the kind of quantum nudges predicted by CSL. The result did not surprise them. If quantum collapse is an actual physical phenomenon, it is an extraordinarily weak one. The question was: How

weak? Now they have put extremely precise bounds on the effect. "If you apply the model to the mirror at LIGO, the mirror should move more than expected, but the mirror doesn't move much. Therefore, the collapse noise can't be too strong," Bassi says.

Physicists have also hunted for signs of collapse in experiments designed to look for dark matter—hypothetical particles thought to account for up to 85 percent of the matter in the universe. One such experiment, sheltered in the Spanish Pyrenees, uses germanium detectors to search for signs of dark matter particles zipping through and generating a flash of x-rays. A collapsing wave function should likewise create a flash, but experimenters have seen no such emissions.

These types of experiments have tightened the constraints on collapse models considerably but not fatally. Last September, Andrea Vinante, a physicist at the University of Southampton in England, along with Bassi and three colleagues, reported the discovery of tentative evidence in support of the CSL model. Vinante's team constructed a miniature cantilever (a horizontal beam fixed at one end), just half a millimeter long and two microns thick and tipped with a small magnet. The researchers carefully shielded the setup from any external vibrations and cooled the cantilever to 40 thousandths of a kelvin above absolute zero to eliminate any possibility of thermally induced movements.

Under those conditions the cantilever should have vibrated ever so slightly because of thermal motion of its particles. But the actual wobble was greater than this predictable motion. The experiment's motion detector—an extremely sensitive instrument called a superconducting quantum-interference device, or SQUID—found that the cantilever and its magnet vibrated like a diving board, bending up and down by a few trillionths of a meter. Eleven years ago Adler calculated that collapsing wave functions might produce vibrations of approximately that size.

"We could see some unexplained noise," says Vinante, describing his experimental results. "It's something that is consistent with what we expect from collapse models, but it could be from an effect we have not understood completely." He and his colleagues are working on upgrades to improve the experiment's sensitivity by at least a factor of 10 and perhaps a factor of 100. "We should be able to either confirm that there is something anomalous or rule out that what we observed was anything interesting," Vinante says it might take another year or two before they have new data. Given the century-long track record of quantum theory's dominance, the odds of discovering a deviation are slim.

But what if one of these experiments does pan out and confirms the phenomenon of quantum collapse? Would that mean an end to the mysteries and paradoxes of the theory? "If collapse really existed, it would divide the world into different scales," says

Igor Pikovski, a theoretical physicist at the Harvard-Smithsonian Center for Astrophysics. "Above a certain scale quantum mechanics would cease to be the correct theory. But below that scale everything we know about quantum mechanics would still hold. So the same philosophical questions and interpretations that bug us would still hold for the lower scale. You'd still have many worlds for electrons or atoms—but not for the moon! So it doesn't solve some of the problems—I think it makes it more strange."

Models such as CSL are just preliminary efforts to unify those two realms. Although they are not full-fledged theories yet, they may eventually help physicists develop a more comprehensive model of reality than quantum mechanics now provides. "My own belief is that you need some modification of quantum mechanics," Adler says. "I don't see why that is a problem. Newtonian mechanics was believed to be exact for 200 years, and it's not. Most theories have a domain in which they work, and then there's a domain beyond which they don't work and where a broader theory is needed."

But for now, at least, quantum mechanics largely seems to withstand every test. "No, we're not facing any crisis. That's the problem!" Weinberg says. "In the past, we made progress when existing theories ran into difficulties. There's nothing like that with quantum mechanics. It's not in conflict with observation at all. It's a problem of failing to satisfy the reactionary philosophical preconceptions of people like me."

Yet for all the weirdness of quantum mechanics, most scientists are happy to leave it be. They carry on using the theory to operate their atom smashers and dark matter detectors and rarely stop to ponder what quantum mechanics says—or does not say—about the fundamental nature of reality. "I think most physicists have what seems to me a very healthy attitude," Weinberg says, "to go on using it, to try to push forward the frontiers of our knowledge and leave the philosophical questions for a future generation." More than a few, though, are not willing to wait that long. "Some people will tell you quantum mechanics has taught us that the world is strange, so we have to accept it," Bassi says. "I would say no. If something is strange, then we have to understand better." ■

MORE TO EXPLORE

Mechanical Resonators for Quantum Optomechanics Experiments at Room Temperature. R. A. Norte et al. in *Physical Review Letters*, Vol. 116, No. 14, Article No. 147202; April 8, 2016. Preprint available at <https://arxiv.org/abs/1511.06235>

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FROM OUR ARCHIVES

Was Einstein Right? George Musser; September 2004.

Quantum Weirdness? It's All in Your Mind. Hans Christian von Baeyer; June 2013.

scientificamerican.com/magazine/sa



PSYCHOLOGY

THE SCIENCE OF ANTI- SCIENCE THINKING

Convincing people who doubt the validity of climate change and evolution to change their beliefs requires overcoming a set of ingrained cognitive biases

*By Douglas T. Kenrick, Adam B. Cohen, Steven L. Neuberg
and Robert B. Cialdini*

IN BRIEF

Scientific thinking often encounters ambivalent responses. Acclaim follows the arrival of heavier-than-air flying machines or the smartphone. But a finding challenging the political or religious status quo can trigger censure and opposition.

How do the results of evidence-based research get the hearing that they deserve? Simply presenting a litany of facts is not enough. In fact, this approach can backfire because of humans' propensity to forgo rational decision making.

Psychologists who study thinking patterns have devised strategies to counteract our tendency to take mental shortcuts, to reinforce preexisting beliefs and to succumb to the pressures exerted by other members of the various groups to which we belong.

IN PRINCIPLE, SCIENCE SHOULD SET ITSELF APART FROM THE HUE AND CRY OF PARTISAN BICKERING. After all, the scientific enterprise reaches its conclusions by testing theories about the workings of the natural world. Consider the porpoise. Based on its appearance and aquatic home, the animal was assumed to be a fish. But evidence gleaned from observing its bone structure, its lack of gills and the genes it holds in common with other warm-blooded land animals leads to its being classified as a mammal with a very high level of confidence.

Yet a consensus about what constitutes a fact does not always come so readily. Take a glance at your online news feed. On a regular basis, government decision makers enact policies that fail to heed decades of evidence on climate change. In public opinion surveys, a majority of Americans choose not to accept more than a century of evidence on evolution by natural selection. Academic intellectuals put the word “science” in quotes, and members of the lay public reject vaccinations for their children.

Scientific findings have long met with ambivalent responses: A welcome mat rolls out instantly for horseless buggies or the latest smartphones. But hostility arises just as quickly when scientists’ findings challenge the political or religious status quo. Some of the British clergy strongly resisted Charles Darwin’s theory of evolution by natural selection. Samuel Wilberforce, bishop of Oxford, asked natural selection proponent Thomas Huxley, known as “Darwin’s bulldog,” on which side of his family Huxley claimed descent from an ape.

In Galileo’s time, officials of the Roman Catholic Church, well-educated and progressive intellectuals in most respects, expressed outrage when the Renaissance scientist reported celestial observations that questioned the prevailing belief that Earth was the center of the universe. Galileo was placed under house arrest and forced to recant his views as heresy.

In principle, scientific thinking should lead to decisions based on consideration of all available information on a given question. When scientists encounter arguments not firmly grounded in logic and empirical evidence, they often presume that purveyors of those alternative views either are ignorant of the facts or are attempting to discourage their distribution for self-serving reasons—tobacco company executives suppressing findings linking tobacco use to lung cancer, for instance. Faced with irrational or tendentious opponents, scientists often grow increasingly strident. They respond by stating the facts more loudly and clearly in the hope that their interlocutors will make more educated decisions.

Several lines of research, however, reveal that simply presenting a litany of facts does not always lead to more objective decision making. Indeed, in some cases, this approach might actually backfire. Human beings are intelligent creatures, capable of masterful intellectual accomplishments. Unfortunately, we are not completely rational decision makers.

Understanding why people engage in irrational thinking requires combining knowledge from a range of psychological disciplines. As authors, each of us studies a separate area addressing how biased views originate. One of us (Cialdini) has expertise in heuristics, the rules that help us to quickly make everyday choices. Another of the authors (Kenrick) has studied how decisions are distorted by social motives such as the desire to find a mate or protect oneself from physical harm.

Yet another of us—Cohen—has investigated how religious beliefs affect judgment. Finally, Neberg has studied simple cognitive biases that lead people to hold on to existing beliefs when confronted with new and conflicting evidence. All of us, in different ways, have tried to develop a deeper understanding of the psychological mechanisms that warp rationality.

Explaining why thinking goes astray is critically important to dispel false beliefs that circulate among politicians, students or even misinformed neighbors. Our own research and that of our colleagues have identified key obstacles that stand in the way of clear scientific thought. We have investigated why they arise and how they might be challenged and ultimately knocked down. Among the many hurdles, three in particular stand out:

Shortcuts. Human brains are endowed with a facile means for dealing with information overload. When we are overwhelmed or are too short on time, we rely on simple heuristics, such as accepting the group consensus or trusting an expert.

Confirmation Bias. Even with ample time and sufficient interest to move beyond shortcuts, we sometimes process information in a manner less like an impartial judge and more like a lawyer working for the mob. We show a natural tendency to pay attention to some findings over others and to reinterpret mixed evidence to fit with preexisting beliefs.

Social Goals. Even if we surmount the first two obstacles, powerful forms of social motivation can interfere with an objective analysis of the facts at hand. Whether one is biased toward reaching one scientific conclusion versus another can be influenced by the desire to win status, to conform to the views of a social network or even to attract a mate.

BEWARE THE SHORTCUT

MASTERY OF THE SCIENCES requires dealing with a set of difficult concepts. Take Darwin’s theory of natural selection. To under-



MARCH FOR SCIENCE in Los Angeles, one of many held last year, tried to bolster support for the scientific community and for dealing with issues such as climate change. Pro-Trump counterdemonstrators also rallied.

stand it, one must comprehend a set of logical premises—that limited resources favor individuals who are better able to procure food, shelter and mates, thereby leading to selective representation of traits that confer these skills to future generations. The student of Darwinian theory must also know something about comparative anatomy (whales have bone structures more similar to humans than they do to fish). Another prerequisite is a familiarity with ecology, modern genetics and the fossil record.

Although natural selection stands out as one of the most solidly supported scientific theories ever advanced, the average citizen has not waded through textbooks full of evidence on the topic. In fact, many of those who have earned doctorates in scientific fields, even for medical research, have never taken a formal course in evolutionary biology. In the face of these challenges, most people rely on mental shortcuts or the pronouncements of experts, both strategies that can lead them astray. They may also rely—at their own peril—on intuition and gut instinct.

We use heuristics because they frequently work quite well. If a computer malfunctions, users can spend months learning about its various electronic components and how they are connected—or they can ask a computer technician. If a child develops a serious health problem, parents can study the medical literature or consult a physician.

But sometimes shortcuts serve us poorly. Consider a classic 1966 study by psychiatrist Charles K. Hofling and his colleagues on how things can go terribly wrong when people rely on the title “Dr.” as a cue to an individual’s authority. In the study, nurses working on a busy hospital ward received a phone call from a man who identified himself as the physician of a patient on their floor. The stranger on the phone asked the nurses

on duty to go to the medicine cabinet and retrieve an unfamiliar drug called Astroten and to administer a dose twice as high as the daily maximum, violating not only the boldly stated guidelines on the label but also a hospital policy requiring handwritten prescriptions. Did the nurses balk? Ninety-five percent obeyed the unknown “doctor” without raising any questions. Indeed, they had to be stopped on their way to the patient’s room with the potentially dangerous drug in hand. The nurses had unknowingly applied what is known as the authority heuristic, trusting too readily in a person in a position of responsibility.

CONFIRMATION BIAS

WHEN WE CARE ENOUGH about a topic and have the time to think about it, we move beyond simple heuristics to a more systematic analysis of the actual evidence. But even when we try hard to retain an objective perspective, our existing knowledge may still get in the way.

Abundant evidence suggests that people pay selective attention to arguments that simply reinforce their own viewpoints. They find disagreement unpleasant and are inclined to dislike the bearer of positions that run counter to their current beliefs. But what happens if intelligent individuals are forced to consider evidence on both sides of an issue?

In 1979 Charles Lord, then at Stanford University, and his colleagues conducted a study with Stanford students, who should have been able to make reasonable judgments about scientific information. The students were exposed to several rounds of scientific evidence on the deterrence of the death penalty. They might first read a description of a study that questioned whether capital punishment prevents serious crime. It compared murder rates for the year before



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and the year after the implementation of capital punishment in 14 states. In 11 of the states, murder rates climbed after the death penalty was established, implying that it lacks a deterrent effect.

Next, the students heard arguments from other scientists about possible weaknesses in that study's evidence. Then the original researchers came back with counterarguments. After that, the students heard about a different type of study suggesting the opposite: that capital punishment stops others from committing crimes. In it, researchers compared murder rates in 10 pairs of neighboring states with different capital punishment laws. In eight of the paired states, murder rates notched lower with capital punishment on the books, supporting the death penalty. Then students heard that evidence challenged, followed by a counterargument to that challenge.

If the students began with a strong opinion one way or the other and then performed a cold, rational analysis of the facts, they might have been expected to gravitate toward a middle ground in their views, having just heard a mix of evidence that included scientific claims that contradicted both positions for and against capital punishment. But that is not what happened. Rather students who previously favored the death penalty became even more disposed toward it, and opponents of it turned more disapproving. It became clear that students on either side of the issue had not processed the information in an evenhanded manner. Instead they believed evidence that reinforced their position was stronger, whereas refutations of that evidence were weak. So even if counterarguments can make it past our inner censors, we show an inclination to weigh those arguments in a very biased manner.

A more recent study by Anthony N. Washburn and Linda J. Skitka, both at the University of Illinois at Chicago, seems to reinforce the Stanford paper's findings. The investigators tested the theory that conservatives are more distrustful of scientific evidence than liberals, perhaps because such individuals exhibit rigid thinking and are less open to new experiences. What they discovered, though, is that those on both the right and left reject scientific findings that do not jibe with their own political ideologies. The authors gave 1,347 study participants scientific evidence on six hot-button issues—climate change, gun control, health care reform, immigration, nuclear power and same-sex marriage. A cursory look at the evidence from scientific studies tended to favor one side of the issue—the absolute numbers of crimes in cities with stricter gun control might be higher than in cities without it. But a closer look at the data might give credence to the opposite view—percentage crime reductions in those same cities might actually be greater than they were for cities lacking gun-control laws.

If the initial hasty inspection of the data tended to favor the anti-gun-control group's expectations, members would generally look no further, content with finding results that supported their particular bias. If the results contradicted the beliefs of the gun advocates, they would scrutinize the details of the study until they discovered the numbers that suggested the opposite conclusion. If the researchers, moreover, later told one of the groups that results favored the opposite side, its members tended to be skeptical of the scientists who conducted the studies.

THE SOCIAL PRESSURE GAUNTLET

ADDITIONAL OBSTACLES ARISE from the same powerful social impulses that help us get along with others. Take the scenario of an office party where an individual's co-workers sound off erroneous claims about evolution, global warming or evidence linking vaccines to autism. Confronted with that situation, does one object or keep quiet to avoid seeming disruptive?

Research on conformity runs deep in the psychological annals. In a classic 1951 study of group dynamics, psychologist Stanley Schachter observed what happened to an individual who disagreed with the majority's consensus. After trying unsuccessfully to change the divergent opinion, other group members ended up cutting off any further communication, ostracizing the outlier. A 2003 functional magnetic resonance imaging study by Kipling D. Williams, now at Purdue University, and his

Even if the human mind has many obstacles to objective thinking, we shouldn't accept that ignorance and bias will always triumph. Social psychology suggests ways of coping.

colleagues found that ostracism activates the brain's dorsal anterior cingulate cortex—the same region recruited when experiencing physical pain. In a 2005 study, a team of researchers led by Gregory Berns, a neuroeconomics professor at Emory University, and his colleagues found that disagreeing with a group to which you belong is associated with increased activity in the amygdala, an area that turns on in response to different types of stress. Holding an opinion different from other group members, even a correct one, hurts emotionally. It therefore comes as no surprise that people are often reluctant to provide evidence counter to what the rest of their group believes.

Social pressures can also influence how we process new information. Group consensus may encourage us to take recourse in heuristics or to cling tightly to an opinion, all of which can interfere with objective thinking.

Our own research team conducted a study in which participants would make aesthetic judgments about a series of abstract designs and paintings and then read a passage designed to put them in either a self-protective or a romantic frame of mind. In the former condition, you might be asked to imagine being awakened by a loud sound while alone at home. As the scenario unfolded, it becomes clear that an intruder has entered the house. You imagine reaching for the phone but finding that the line is dead. A call for help receives no response. Suddenly, the door to the bedroom bursts open to reveal the dark shadow of a stranger standing there.

Alternatively, you might be randomly assigned to read an account of a romantic encounter and asked to imagine being on vacation and meeting an attractive person, then spending a romantic day with the partner that ends with a passionate kiss. Next you would enter a virtual chat room, joining three other participants to evaluate abstract images, including one you had earlier judged as of average interest. Before making the second

judgment, though, you learn that this image has been rated as way below average by the other subjects.

So did study subjects change their initial judgment to conform to the other group members? How people responded depended on their current goals. Study participants who had read the home break-in scenario were more likely to conform to the group judgment. In contrast, those exposed to the amorous story answered differently depending on gender: women conformed, but men actually went against the group's judgment.

Other studies by our team have found that fear can lead both men and women to comply with group opinion, whereas sexual motives prompt men to try to stand out from the group, perhaps to show that they are worthy mates. Men, in this frame of mind, are more likely to challenge the consensus and increase the riskiness of their actions. In all cases, though, our participants' views were shaped by their social goals in the moment. They did not process available information in a completely objective way.

WHAT TO DO

IF THE HUMAN MIND is built with so many obstacles to objective scientific thinking, should we just give up and accept that ignorance and bias will always triumph? Not at all. Research in social psychology also suggests ways of coping with heuristics, confirmation biases and social pressures.

We have seen that people frequently rely on heuristics when they lack the time or interest to carefully consider the evidence. But such rules of thumb can often be defeated with simple interventions. In one experiment by market researchers Joseph W. Alba and Howard Marmorstein, subjects considered information about a dozen separate features of two cameras. Brand A was superior to brand B on just four of the features, but these were features critical in considering camera quality—the exposure accuracy, for instance. Brand B, on the other hand, came recommended as superior on eight features, all of which were relatively unimportant—having a shoulder strap, for example. Some subjects examined each attribute for only two seconds; others had more time to study all the information.

When they had only two seconds to evaluate each feature, only a few subjects (17 percent) preferred the higher-quality camera, most opting instead for the one with a greater number of unimportant functions. When the subjects were given sufficient time and allowed to directly compare the two cameras, however, more than two thirds favored the camera with the few features key to its overall quality. These results suggest that when communicating complicated evidence, sufficient time is needed to switch from a heuristic to a systematic mode of thinking that allows for better overall evaluation.

Confirmation biases can often be overcome by changing one's perspective. The same Stanford researchers who studied attitudes toward capital punishment also investigated how to change them. They instructed some students to remain objective and weigh evidence impartially in making a hypothetical decision related to the death penalty. That instruction had no effect. Other students were asked to play their own devil's advocate by considering what their opinions would have been if the research about the death penalty had contradicted their own views. Biases suddenly vanished—students no longer used new evidence to bolster existing preconceptions.

One way to counteract social pressures requires first explor-

ing whether agreement within the group really exists. Someone who disagrees with an erroneous opinion can sometimes open other group members' minds. In a 1955 *Scientific American* article, social psychologist Solomon E. Asch described studies on conformity, finding that if a single person in the group disagreed with the majority, consensus broke down. Similarly, in Stanley Milgram's famed studies of obedience—in which participants were led to believe that they were delivering painful shocks to an individual with a heart problem—blind obedience dissipated if other team members chose not to obey.

Fear increases the tendency toward conformity. If you wish to persuade others to reduce carbon emissions, take care whom you scare: a message that arouses fear of a dystopian future might work well for an audience that accepts the reality of climate change but is likely to backfire for a skeptical audience.

We have provided a few simple suggestions for overcoming psychological obstacles to objective scientific thinking. There is a large literature on persuasion and social influence that could be quite useful to anyone attempting to communicate with a group holding beliefs that fly in the face of scientific evidence. For their part, scientists need to adopt a more systematic approach in collecting their own data on the effectiveness of different strategies for confronting antiscientific thinking about particular issues. It is essential to understand whether an individual's resistance to solid evidence is based on simple heuristic thinking, systematic bias or particular social motives.

These steps are critical because antiscientific beliefs can lead to reduced research funding and a consequent failure to fully understand potentially important phenomena that affect public welfare. In recent decades government funding has decreased for research into the health impact of keeping guns in the home and of reducing the harmful effects of air pollution. Guns in the home are frequently involved in teenage suicides, and an overwhelming scientific consensus shows that immediate measures are needed to address the planet's warming.

It is easy to feel helpless in the face of our reluctance to embrace novel scientific findings. Still, there is room for optimism: the majority of Galileo's fellow Italians and even the pope now accept that our planet revolves around the sun, and most of Darwin's compatriots today endorse the theory of evolution. Indeed, the Anglican church's director of public affairs wrote an apology to Darwin for the 200th anniversary of his birth. If scientists can incorporate the insights of research on the psychological obstacles to objective thinking, more people will accept objective evidence of how the natural world functions as well. ■

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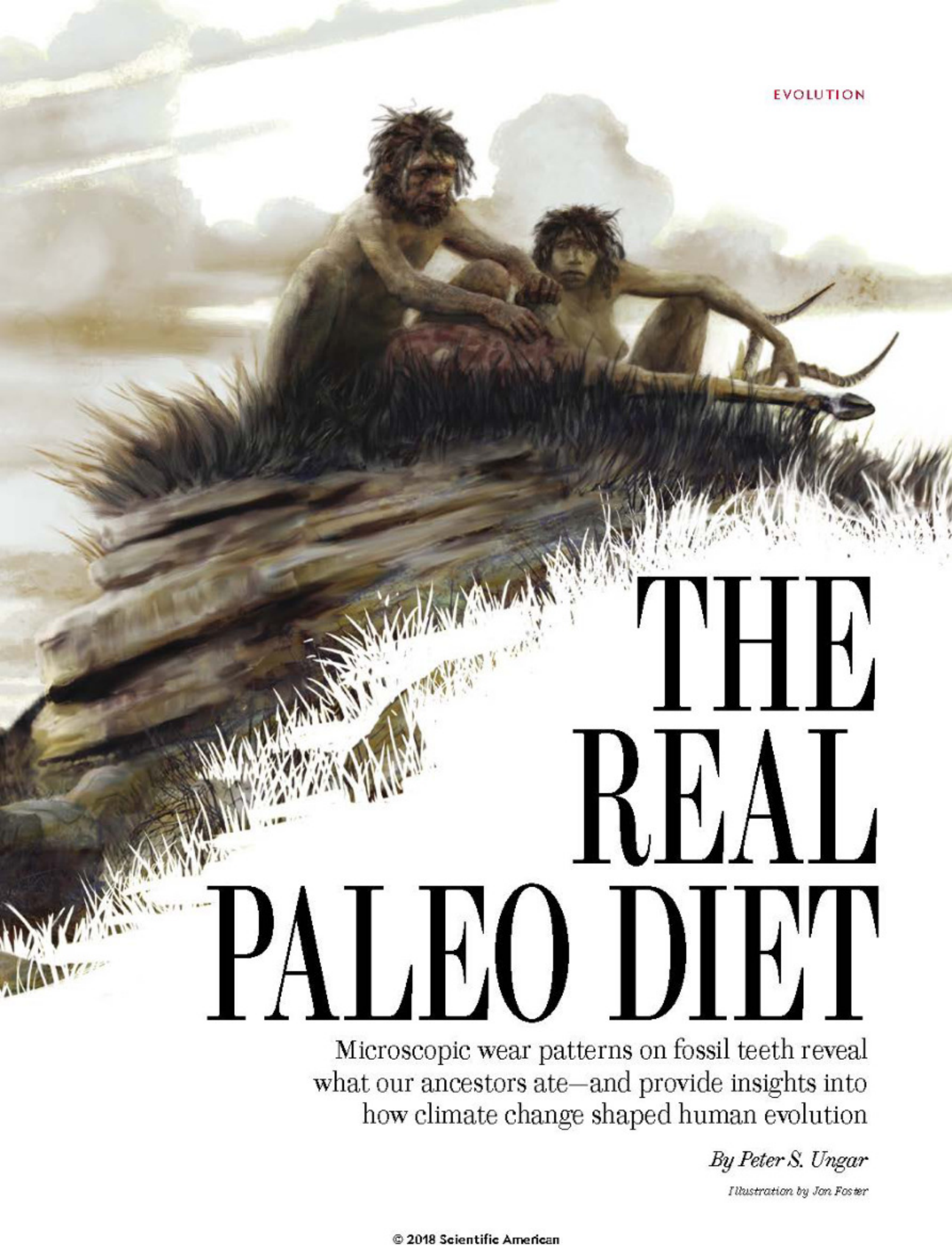
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EVOLUTION

THE REAL PALEO DIET

Microscopic wear patterns on fossil teeth reveal what our ancestors ate—and provide insights into how climate change shaped human evolution

By Peter S. Ungar

Illustration by Jon Foster

Peter S. Ungar is a paleontologist at the University of Arkansas. His research focuses on diet and feeding adaptations in living and fossil primates, including human ancestors. His most recent book is *Evolution's Bite* (Princeton University Press, 2017).



LATE ONE EVENING IN 1990 AT THE KETAMBE RESEARCH STATION IN INDONESIA'S GUNUNG Leuser National Park, I sat transcribing notes by the light of a kerosene lamp in my hut on the banks of the Alas River. Something was bothering me. I had come to gather data for my dissertation, documenting what and how the monkeys and apes there ate. The idea was to relate those observations to the sizes, shapes and wear patterns of their teeth. Long-tailed macaques have large incisors and blunt molars—teeth built for eating fruit, according to the received wisdom. But the ones I had been tracking for the past four days seemed to eat nothing but young leaves. I realized then that relations between tooth form and function are more complicated than the textbooks suggest and that the sizes and shapes of an animal's teeth do not dictate what it eats. This might sound like an esoteric revelation, but it has key implications for understanding how animals—including humans—evolved.

IN BRIEF

Paleontologists have traditionally assumed that the sizes and shapes of an animal's teeth dictate its diet. But food availability—which changes seasonally and over larger timescales—is an even bigger factor in what an animal chooses to eat. **Analyses of microscopic wear** and chemical traces of food on fossil teeth are going beyond conventional studies of tooth form to reveal what human ancestors truly ate. **The diet findings**, along with paleoenvironmental data, provide fresh insights into how climate change shaped human evolution.

I am a paleontologist, and I earn a living reconstructing the behaviors of extinct species from their fossilized remains. Specifically, I work to discern how animals in the past obtained food from their surroundings and thus how environmental change triggers evolution. That year at Ketambe shaped my way of thinking about primates and the larger community of life that surrounds them. I began to see the biosphere—the part of our planet that harbors life—as a giant buffet of sorts. Animals belly up to the sneeze guard with plates in hand to pick from items available in a given place, at a given time. Each species' place in the forest, and in nature, is defined by the choices it makes.

Teeth play a role in food choice—you need the right utensils. But I learned at Ketambe that availability is even more important. The macaques ate leaves because that is what nature laid out on the biospheric buffet at that time and place. Their diet changed over the course of the year as leaves unfurled, flowers bloomed and fruits ripened with the passing seasons. I began to imagine how changes in food availability over centuries, millennia or longer could affect what a species eats.

Most paleontologists are not used to thinking about life in the past this way. Our field has a long tradition of inferring function from form by assuming that nature selects the best tools for whatever job an organism has to do. If form always followed function, however, macaques would not eat leaves. But how can we detect food choices in the fossil record?

I have spent decades doing exactly that by studying microscopic wear patterns on fossil teeth, including those of a number of human ancestors. Other researchers have analyzed the chemical signatures of food in fossil teeth for dietary clues. These “foodprints,” as I call them, reveal the kinds of foods individuals actually ate and have given us a much richer picture of the past than tooth shape alone. Together with insights from the paleoenvironmental record, these findings have allowed us to test some leading hypotheses about the impact of climate change on human evolution. The results refine the classic explanation for how our branch of the human family tree succeeded where others did not.

LIEM'S PARADOX

OBSERVATIONS OF LIVING ANIMALS have revealed numerous creatures that eat foods other than the ones to which they are adapted. While I was at Ketambe, Melissa Remis, now at Purdue University, was gathering diet data on gorillas at Bai Hokou, a lowland rain forest site in the Central African Republic's Dzanga-Ndoki National Park. At that time, most researchers thought that gorillas were dietary specialists that ate stems, leaves and the pith of nonwoody plants such as wild celery. Pioneering gorilla researcher Dian Fossey and others had shown as much in the high-altitude cloud forests of the Virunga Mountains in Uganda and Rwanda. It made sense. Gorillas have very spe-

cialized teeth and guts—sharp-crested molars well suited to shearing tough plant parts and a massive hindgut to host microorganisms that help to digest cellulose in fibrous foods. Besides, there was little else to eat at those elevations.

The Virunga mountain gorillas were actually a small, marginal population of just a few hundred individuals living in an extreme habitat, however. What about the 200,000 gorillas living 1,000 miles to the west in the lowland rain forests of the Congo Basin? The gorillas at Bai Hokou told a different story. They seemed to prefer soft, sugary fruits. In fact, Remis saw gorillas walk half a mile or more, right past edible leaves and stems, to get to a fruiting tree. Fibrous foods seemed to dominate their diet only when favored fruits were unavailable. But western lowland gorillas were skittish compared with their cousins in the Virunga Mountains, limiting the amount of data Remis could collect. Some researchers questioned whether gorillas could actually prefer fruits, given their teeth and guts.

There is an old joke: "What do you feed a 400-pound gorilla? Anything it wants." How can we know what a gorilla wants to eat? After Remis returned home from Bai Hokou, she went to the San Francisco Zoo to ask the gorillas themselves. She offered the captive apes a variety of foods, from sweet mango to bitter tamarind, sour lemon and, of course, tough celery. The zoo gorillas clearly preferred sugary, fleshy fruits to tough, fibrous foods, regardless of what their teeth and guts suggested they should eat. This finding confirmed that although gorillas are adapted to the most mechanically and chemically challenging foods they have to eat, these are not their favored foods. Perhaps, then, gorillas in the Virunga Mountains eat tough, fibrous foods year-round not because they prefer them but because they can—and must, given the limited options on the biospheric buffet at such high elevations. Indeed, nearby mountain gorillas that live at lower altitudes prefer to eat fruit when it is available.

A preference for foods other than those to which one is adapted is common enough in the animal kingdom to merit a term for the phenomenon: Liem's paradox. The late Karel Liem of Harvard University observed the paradox first in 1980 in Minckley's cichlid, a freshwater fish endemic to the valley of Cuatro Ciénegas in northern Mexico. One form of this fish has flat, pebblelike teeth in its throat that are seemingly perfectly suited for cracking hard-shelled snails. Yet members of this group swim right past those snails when softer foods are available. Why would an animal evolve teeth specialized for less preferred, rarely eaten items? So long as the hard-object specialization does not preclude consumption of softer foods, it can leave an animal more options when it needs them. The paradox, then, is not so much that individuals avoid the foods to which they are adapted but that specialized anatomy can lead to a more generalized diet.

Other primates exemplify Liem's paradox, including



the gray-cheeked mangabey monkeys of Uganda's Kibale National Park. Mangabeys have flat, thickly enameled molars that seem to be specialized for crushing hard, brittle foods. But day after day, month after month, even year after year, Joanna Lambert, now at the University of Colorado Boulder, watched them eat soft, fleshy fruits and young leaves, just like the thinner-toothed red-tailed guenon monkeys that lived alongside them. Then, in the summer of 1997, everything changed. The forest was reeling from an especially severe drought brought on by an El Niño event. Fruits were scarce, leaves were wilting and the monkeys were hungry. The mangabeys ate more bark and hard seeds, but the guenons did not. The mangabeys' specialized teeth and jaws allowed them to fall back on mechanically challenging foods. Even if such adaptations are needed only once or twice in a generation, that can be just what the animals require to get through the lean times.

Specialized anatomy can also relate to preferred foods, though. Sooty mangabeys in Ivory Coast's Tai National Park, for instance, have thick tooth enamel

GRAY-CHEEKED MANGABEYS have flat, thickly enameled molars that appear to be specialized for crushing hard foods. But they only fall back on these foods when the soft fruits and leaves they prefer are unavailable.

and strong jaws, and they actually prefer hard foods. Much of their foraging time is devoted to scouring the forest floor for seeds of the *Sacoglottis* tree, which have casings that resemble peach pits. Scott McGraw of Ohio State University argues that this practice allows them to avoid competing for food with the 10 other primate species that live alongside them. Just as gorillas vary in how often they eat mechanically challenging foods, some mangabeys eat them all the time, and others do so only on rare occasions.

Examples such as these show that primate food choice is complex and depends not just on teeth but also on availability, competition and personal preference. Tooth form can tell us something about what an animal in the past was capable of eating and the most challenging foods its ancestors had to contend with. But for insights into food choices among options that were available on the biospheric buffet, we need foodprints.

Dental microwear, the microscopic scratches and pits that form on a tooth's surface as the result of its use, is a commonly studied type of foodprint. Species that tend to shear or slice tough foods, such as grass-grazing antelopes or meat-eating cheetahs, get long, parallel scratches as opposing teeth slide past one another and abrasives between them are dragged along. Species that crush hard foods, such as nut-eating Taï mangabeys or bone-crunching hyenas, tend to have cratered microwear surfaces, covered in pits of various sizes and shapes.

Because those marks typically wear away and are overwritten in a matter of days, we can learn something about the variety, and perhaps even the proportions, of foods eaten if we consider teeth of individuals sampled at different times and places. The microwear patterns of Kibale mangabeys typically resemble those of soft-fruit eaters, with wispy scratches and fine pits, although a few specimens are more heavily pitted. The teeth of mangabeys from Taï, in contrast, have much more cratered surfaces on average. Despite similar tooth form in the two species, foodprints distinguish them as predicted, based on observations of their diets.

ANCIENT MENUS

WITH MICROWEAR PATTERNS from living animals whose dietary habits are known from firsthand observation to guide us, scientists can use microwear on fossil teeth to infer what extinct species ate on a daily basis and gain insight into their food choices. To that end, my colleagues and I have put a lot of effort into analyzing

the microwear of human fossils. Our work has generated surprising results.

The human family tree has many branches. Today *Homo sapiens* is the only human species alive, but once upon a time, multiple human species, or hominins, shared the planet. Why our lineage survived when others went extinct is an enduring question. My own foray into this mystery began when I set out to study the diet of members of one of these extinct branches, a group of species belonging to the genus *Paranthropus*. *Paranthropus* lived in eastern and southern Africa between about 2.7 million and 1.2 million years ago, during the Pleistocene epoch. None of its species gave rise to us; rather they were evolutionary experiments that walked alongside our own early ancestors. *Paranthropus* had big, flat, thick-enameled premolars and molars, heavy jaws, and the telltale bony ridges and scars that come from having massive, powerful chewing muscles. These traits are clearly dietary specializations for extreme chewing, so these species seemed to be ideal candidates for microwear analysis. If my collaborators and I could not figure out what they ate, then we had little hope of reconstructing diets of other fossil hominins with less distinctive jaws and teeth.

Paleoanthropologist John Robinson was the first to try to reconstruct the diet of *Paranthropus*, back in 1954. Robinson believed that the

large, flat and thickly enameled premolars and molars of *Paranthropus robustus* from South Africa had evolved for grinding plant parts, such as shoots and leaves, berries and tough wild fruits. Chipping on those teeth suggested to him that *P. robustus* ate grit-laden roots and bulbs. The late Phillip Tobias of the University of the Witwatersrand, Johannesburg, saw things differently, arguing in the 1960s that the chips occurred during consumption of hard foods rather than gritty ones. At the time, Tobias was describing a new species of *Paranthropus* from East Africa, *Paranthropus boisei*. On first seeing its skull, he is famously reported to have said, "I have never seen a more remarkable set of nutcrackers."

The idea of a hominin that specialized in nut cracking was born. *Paranthropus* stood in sharp contrast to early *Homo* fossils found in the same sedimentary deposits, with their daintier teeth and jaws, larger brain and emerging stone tool kit for processing food. Researchers came up with a tidy explanation for the differences, dubbed the savanna hypothesis. As grasslands began to spread across Africa, our ancestors came to an evolutionary fork in the road. *Paranthro-*

Tooth form can tell us something about what an animal in the past was capable of eating and the most challenging foods its ancestors had to contend with. But for insights into food choices among options that were available on the biospheric buffet, we need foodprints.

pus went one way, evolving to specialize on hard, dry savanna plant parts, such as seeds and roots. Early *Homo* went another direction, becoming increasingly versatile, with a more flexible diet that included meat. That dietary flexibility is why we are here today and *Paranthropus* is gone, according to the theory. It was a compelling story, and early microwear studies by Frederick Grine of Stony Brook University in the 1980s showed that the teeth of *P. robustus* do have more microwear pits than those of its own predecessors, seemingly confirming that this cousin of ours specialized in hard, brittle foods.

But in 2005, when my then postdoctoral fellow Rob Scott and I looked again at *P. robustus* microwear using newer technology, another part of the story began to emerge. Yes, *P. robustus* specimens had more pitted, complex microwear surfaces on average, but some of the specimens we studied had less pitted, simpler textures. In fact, microwear in *P. robustus* varied a lot, suggesting that while some ate hard foods in the days before they died, others did not. To put it another way, the specialized anatomy of *P. robustus* did not mean it was a dietary specialist. This was not a new idea. David Strait, now at Washington University in St. Louis, and Bernard Wood of George Washington University had the year before speculated that *Paranthropus* may well have been an ecological generalist with a flexible diet, based largely on indirect evidence. But our work provided direct evidence for Liem's paradox among the hominins.

A bigger surprise came in 2008, when my colleagues and I looked at the microwear textures of *P. boisei*. This was Tobias's nutcracker, the species with the largest teeth, heaviest jaws and thickest enamel of all the hominins. I expected *P. boisei*'s teeth to have microwear akin to that of the sooty mangabey's, cratered like the surface of the moon. They did not. Surface after surface had wispy scratches running every which way. Not only were these critters not hard-object specialists, but their microwear showed no sign at all of hard foods. The nutcracker hypothesis seemed to fall like a house of cards in a stiff wind. So what was *P. boisei* eating with those big, flat teeth? That would have to wait on another set of foodprints: carbon isotope ratios.

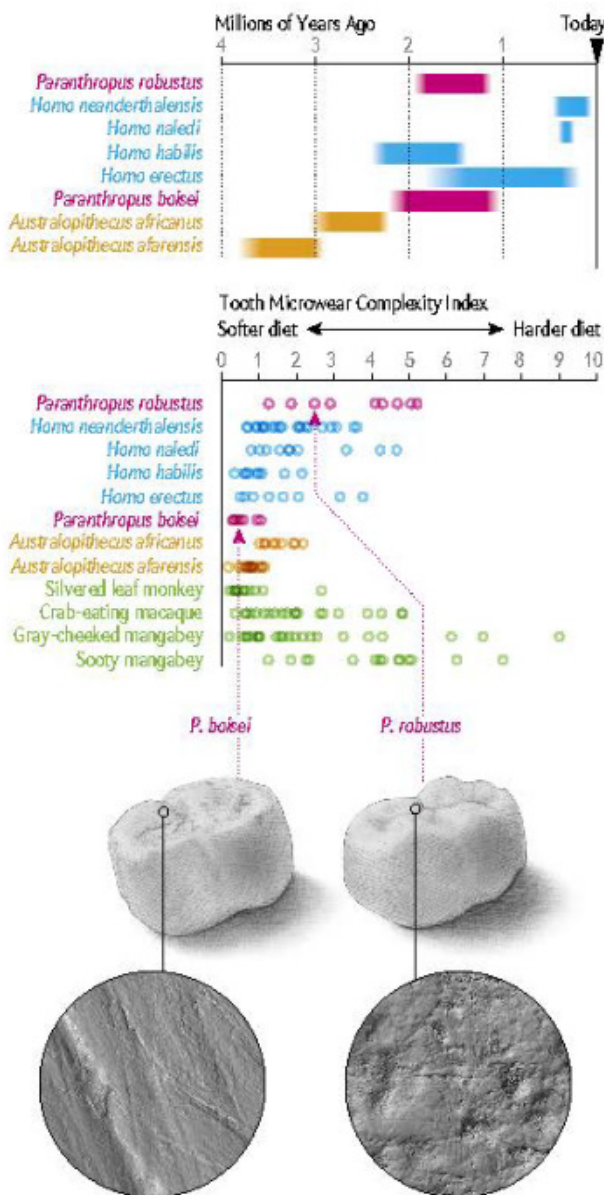
Distinctive chemical signatures of foods that provide the raw materials used to build the body are sometimes preserved in teeth. Like microwear, these chemical clues can be read and decoded. For example, compared with trees and bushes, tropical grasses have a higher proportion of carbon atoms with seven neutrons rather than the usual six; the teeth of animals that eat tropical grasses have predictably more "heavy" carbon as a result.

Carbon isotope ratios of *P. robustus* teeth indicate a diet dominated by tree and bush products but with a hearty helping of tropical grasses or sedges. This finding is consistent with a broad-based diet. But *P. boisei* shows a very different pattern, with carbon isotope ratios suggesting that grasses or sedges made up at least three quarters of its diet.

This result came as a surprise to many paleoanthropologists. A cowlike hominin? Surely no self-respecting member of our family tree would earn its living eating grass! But it made sense to me. These species debuted just as grasslands were spreading across eastern and southern Africa, and the biospheric buffet table was becoming covered in turf. If

Foodprints

Microscopic scratches and pits form on teeth as a result of their use. Studies of these microwear patterns in living animals show that species that chew soft and tough foods such as grass, for example, get long, parallel scratches on their teeth; those that crush hard and brittle foods such as nuts get pits. Paleontologists have inferred the diet of extinct human species, including *Paranthropus robustus* and *Paranthropus boisei*, based on the microwear textures on fossil teeth.



Previous studies based on tooth form concluded that *P. robustus* ate tough plants and that *P. boisei* specialized in cracking nuts. Microwear analysis, however, reveals that *P. robustus* had a complex pattern of pits and scratches indicative of a dietary generalist. *P. boisei*, for its part, had none of the pits one would expect to see in a nutcracker. Subsequent chemical analyses indicated that *P. boisei* ate mostly grasses or sedges.

1



2



P. boisei was grinding grass or sedge products with its big, flat teeth and powerful jaws rather than crushing hard, brittle foods, that should leave exactly the microwear texture pattern my colleagues and I found. Such a diet would also explain why *P. boisei* wore down its molars so quickly.

You would never know it by just looking at the shapes of their huge, flat teeth, but foodprints suggest that the two *Paranthropus* species used their specialized anatomy in different and unexpected ways. Like the Kibale mangabeys, *P. robustus* seems to have had a generalized diet that included some hard objects. But for *P. boisei*, the relation between teeth and diet seems to have been very different from anything we see in primates today. Big, flat teeth are far from ideal for shredding grass, but one works with what one has. And so long as a grinding platform is better than what hominins had before, it would be selected for even if it is not optimal for the task at hand.

Microwear of our direct ancestors—those in the *Homo* genus—points to a decidedly different dietary strategy. My colleagues and I have looked at two early species: the more “primitive” *Homo habilis*, a smaller-brained hominin that retained some features related to life in the trees, and *Homo erectus*, a larger-brained hominin committed to the ground. Our samples are small because microwear requires pristine teeth, and there are just not that many of them. But they show an interesting pattern. Compared with *Australopithecus afarensis*, its putative ancestor, and *P. boisei*, which lived alongside it, *H. habilis* has a somewhat broader range of microwear textures, from complex pitted surfaces to simple scratched ones. The finding hints that

DIVERGING DIETS: Whereas *Paranthropus boisei* (1) specialized in eating grasses or sedges, its contemporary *Homo habilis* (2) appears to have had a broader diet.

H. habilis ate a wider range of foods than either its predecessors or its contemporaries. Its successor *H. erectus* has even more variable microwear textures, perhaps suggesting a broader diet still.

These results fit neatly with a leading model of how climate change shaped human evolution that has superseded the savanna hypothesis. Work on climate data from deep ocean cores in the mid-1990s by the late geologist Nicholas Shackleton showed there was more to the story of climate change than the savanna hypothesis supposed. Conditions did become cooler and drier over the long term, but there were also short-term climate swings, and those swings became more and more intense over the course of human evolution.

Rick Potts of the Smithsonian Institution reasoned that this unstable climate pattern should favor more versatile species, including hominins—an idea that became known as the variability selection hypothesis. Pleistocene Africa was no place to be a picky eater. For Potts, it was not so much the spread of savanna grasses but the need for flexibility that drove human evolution. In this light, *Homo*’s larger brain and stone tools for processing a variety of foods make sense. They would have allowed our ancestors to survive increasingly intense environmental swings and to keep up as nature more quickly swapped items on and off the biospheric buffet. The increasing variation in microwear complexity from *A. afarensis* to *H. habilis* to *H. erectus* just might be direct evidence of variability selection.

Potts’s idea has held up pretty well in the two decades since he first presented it, although others have built on it, and new details have emerged about how changes to Earth’s landscapes and in its orbit around

the sun have combined to create the conditions under which humans evolved. For example, in 2009 Mark Maslin of University College London and Martin Trauth of the University of Potsdam in Germany suggested that climate swings filled and emptied the spreading lakes in eastern Africa, disrupting life in the rift basins. This flux may have led to fragmentation and dispersal of hominin populations, fueling human evolution. The ability to pursue a more variable diet would have aided survival in such turbulent times.

APPETITE AND EVOLUTION

ALTHOUGH THE AVAILABLE EVIDENCE allows scientists to paint a plausible picture of how early hominins adapted to their changing world, we can only do so with the broadest of brushstrokes. The biggest challenge to understanding how climate change drives evolution is matching specific climate events in the past to changes in the fossil record.

Local environments react to global and even regional climate change in different ways, and our fossil record is simply not complete enough to tell exactly where and when particular species appeared and disappeared. We can be off by 1,000 miles and 100,000 years or more. We might be able to tie the extinction or evolution of a given species to a massive, catastrophic event in Earth's history, such as the asteroid impact in the Yucatán Peninsula that killed off the dinosaurs 66 million years ago. But the climate-related events we associate with human evolution are very different—repeated cycles of cool-dry conditions followed by warm-wet ones. The fact that hominins were probably flexible species capable of adjusting to a broad range of habitats and the foods available within them further obscures the picture. Our best shot at understanding how hominins responded to changing environments thus lies in the more recent past, in places that are exceptionally well studied.

Research published by Sireen El Zaatari of the University of Tübingen in Germany, Kristin Krueger of Loyola University Chicago and their colleagues over the past two years shows how this approach might work. Their studies of the microwear of Neandertals and the anatomically modern humans that supplanted them in Eurasia allow us to revisit the long-standing mystery of this replacement from a fresh perspective. Neandertals ruled Europe and western Asia between about 400,000 and 40,000 years ago. Then they were gone. Paleoanthropologists have been debating what happened and why for more than a century, and even today there is little consensus.

Although popular science often tells a tale of brutish Neandertals living in near-glacial conditions, swaddled in animal hides and gorging lustfully on mammoth and woolly rhinoceros meat, it was not always like that. Neandertals inhabited a wide range of habitats, from cold, dry steppes to warmer, wetter woodlands, and conditions varied over time and space. Recent studies of their molars show that Neandertals living

in more wooded or mixed settings had complex pitted microwear, suggesting that they ate more hard, brittle and perhaps abrasive plant foods. Neandertals that dwelled on the open steppes, in contrast, have less complex molar microwear, which El Zaatari and her colleagues argue reflects a less variable diet composed primarily of soft meat. Krueger, for her part, found differences in incisor microwear between the two groups; she thinks the differences stem from the steppe Neandertals having used their incisors to aid in processing animal hides and the forest Neandertals having eaten a greater variety of foods. Intriguingly these differences hold whether one considers earlier Neandertals or later ones. It seems that Neandertals were flexible feeders with diets that tracked to habitat and associated food availabilities.

The pattern is different, though, for anatomically modern people living in Europe during the last ice age. There is not much difference in molar microwear between those from open habitats and those who occupied habitats containing a mix of open and wooded vegetation, whether one considers earlier or later individuals. Perhaps early modern humans were better able to acquire their preferred foods than Neandertals were when faced with environmental change.

FOOD FOR THOUGHT

STUDIES OF EARLY HUMAN DIETS bear on what people today should eat to be healthy—though perhaps not in the manner popularly envisioned. “Paleolithic diet” gurus argue that we should eat the kinds of foods our ancestors evolved to eat. Many chronic degenerative diseases have been linked to a mismatch between our diets and the fuels our bodies were “designed” to burn, they contend. And it certainly cannot hurt to remind ourselves every now and again that our distant forebears did not eat corn dogs or milkshakes.

That does not mean that we should look to follow a specific Paleolithic diet, however. Foodprints teach us that early hominin diets varied over time and space and that we mostly likely evolved to be flexible eaters, driven by ever changing climates, habitats and food availability. In other words, there was no single ancestral human diet for us to replicate. Dietary versatility allowed our ancestors to spread across the planet and find something to eat on all of Earth's myriad biospheric buffets. It was the key to our evolutionary success. 

MORE TO EXPLORE

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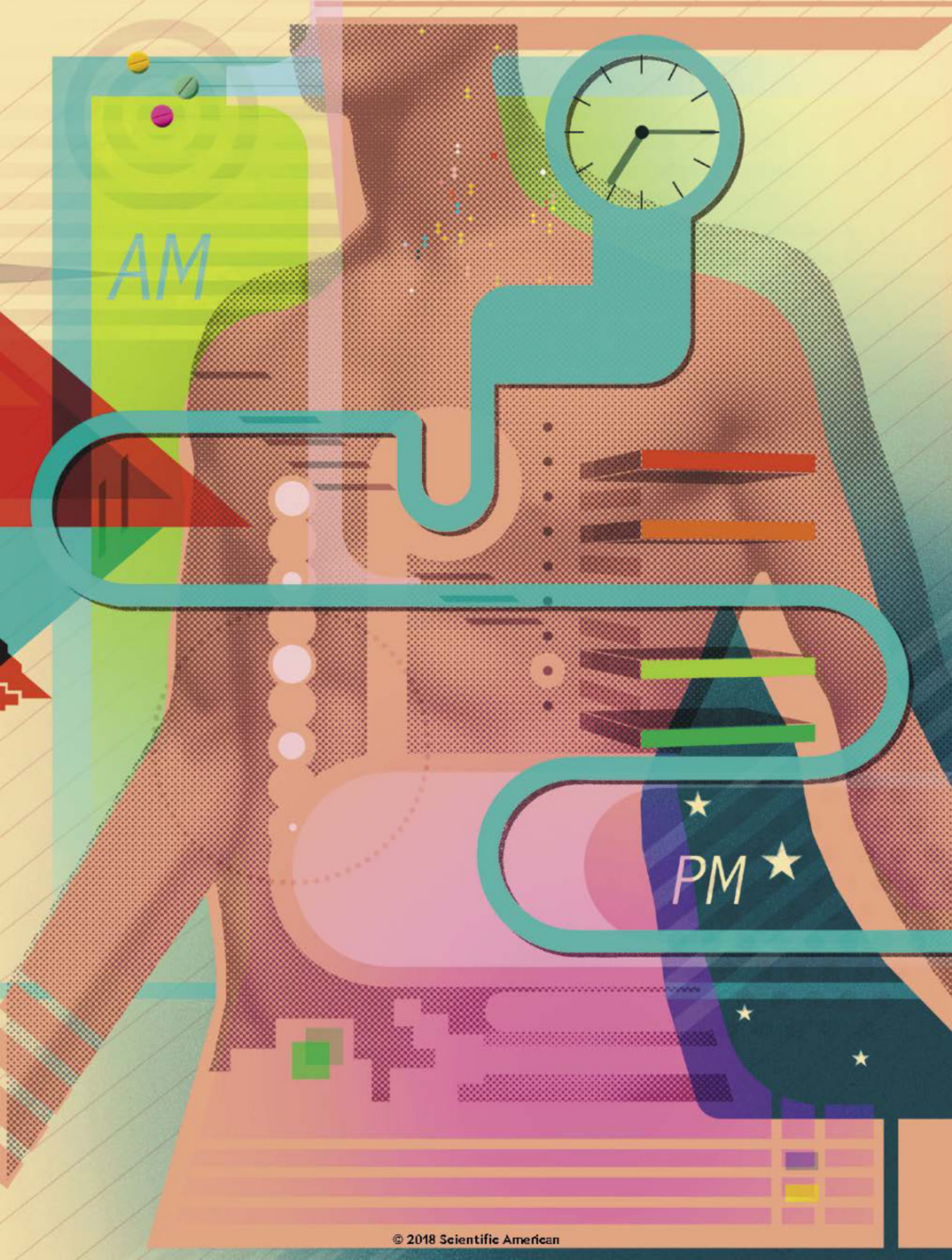
BIOLOGY

How
the body's
cycles
went
from folk
medicine to
modern
science

THE
CLOCKS
WITHIN
OUR
CELLS

By Veronique Greenwood

Illustration by Mark Allen Miller





In the wee hours

of the medieval night, a monk begins to wheeze and cry in fear. His brothers call in the healer, who brings what comfort he can. Asthma is a beast of the nighttime, the healer knows. But in this hypothetical scenario, which might have played out in thousands of darkened bedrooms and dormitories down the years, all the men can do is wait for the symptoms to pass.

IN BRIEF

It is estimated that up to 82 percent of mammalian genes are expressed in a cyclical pattern of highs and lows. This means there is a time aspect to biology.

The implications for medicine are wide-ranging. Fifty-six of the 100 most commonly used drugs target rhythmically expressed proteins, meaning the time of dosing matters.

The emerging field of chronomedicine is testing timed treatments of diseases such as cancer and rheumatoid arthritis to maximize safety and efficacy. **Personalized monitoring** of circadian rhythms may determine different optimal treatment times for each person.

Chronomedicine has not yet reached clinical practice.

Thanks to old medical compendiums, we now know that physicians have long recognized that certain medical disorders exhibit daily variations. Back in the fifth century, Roman doctor Caelius Aurelianus wrote that asthma attacks were more common after dark. In 1568 German physician Christopher Wirsung even pinpointed them as occurring between 2 A.M. and dawn. Blood pressure, heart rate, and the onset of chest pain and heart attacks were observed to have certain rhythms, too.

Of course, those astute observations are recorded alongside suggestions that have long since been relegated to folk medicine. Aurelianus, for instance, instructs readers with sore ears to coat the area with a paste made of saffron, vinegar, myrrh, quince and various other substances that may or may not have helped. Wirsung was quite adamant that foul smells were bad for the heart.

Only centuries later did scientists begin to entertain the possibility that the rhythms of the body could be harnessed for therapeutic benefit. Biologist Franz Halberg was one leader in the effort to study what he called chronobiology, the regular fluctuation of biological measurements over time in individual people and even in individual cells. But first, he and other chronobiologists had to convince their colleagues and the public that chronobiology was serious science. At the time that he gave an interview to *People* magazine in 1978, a system called biorhythms was all the rage—it used your date of birth to generate a trio of lines that purportedly represented an intellectual, physical and emotional status that cycled up and down. The Dallas Cowboys used biorhythms to plan game strategies. Biorhythms appeared to have predicted Clark Gable's

fatal heart attack. And for a while people were even using them to time when they had sex, hoping they could influence the gender of their children.

Halberg stressed that what he studied could not be further from biorhythms, which he called “silly.” “We find cycles in every system of the body,” Halberg, who died in 2013, said to the *People* reporter. “Many more can be discovered, measured and eventually exploited. From the timing of a meal to the administration of an anticancer drug, working with, instead of against, the body's rhythms can tip the scale between health and disease, and even between survival and death.”

The idea initially met with considerable skepticism. It sounded grandiose. How could cancer treatment boil down to timing? The *People* article suggested that some of Halberg's colleagues chalked up his ideas to “paranoia.” It did not make sense to most biologists that time of day would matter. They had gotten perfectly good results in various experiments by doing them whenever it was convenient. And if some tests mysteriously did not give the same results, there could be many explanations.

Today, however, researchers know that time is a real factor in whether an experiment or a treatment succeeds or fails. They are now tracing the circuits by which the time of day writes itself on our bodies, an effort that could help doctors treat a range of diseases more effectively and safely.

CYCLIC PATTERNS OF GENE EXPRESSION

UELI SCHIBLER recalls the day in 1990 when a student walked into his office and said, “You have to retract this paper. It's all fake.” At the time, Schibler, a professor at the University of Geneva, was studying what are

called transcription factors. The DNA that stores all the instructions necessary for life is usually tightly bundled in a cell's nucleus. When there is a call for a particular set of instructions—that is, a gene—then proteins in the nucleus unfurl the relevant segment and transcribe it. The transcript leaves for the outer regions of the cell, where it will be read and used to build a protein. This process is called gene expression. And in it, transcription factors are key.

Transcription factors come in any number of shapes, but their uniting feature is an ability to control how and when transcription happens. They do this by attaching to the DNA itself, among other functions. They too, are proteins made with the use of instructions encoded in genes, lending the entire picture a circular quality. A postdoctoral researcher in Schibler's laboratory had been working on isolating a transcription factor in the liver. It had all seemed to go without a hitch. He found the transcript for the protein DBP in rats, figured out the protein's sequence and identified the gene that made it. Back then, understanding how transcription factors shaped individual tissues was still in its infancy, and characterizing this powerful modulator was an exciting step forward. The researchers published a paper in the prestigious journal *Cell*. "He was happy, and I was happy," Schibler says.

The postdoc went off to his new position as an assistant professor, and a student took over his project. Three months later the student dropped his bombshell: he had repeated the experiment many times, and the transcription factor was never present.

Schibler found it hard to believe his postdoc guilty of fraud, but what other options were there? He immediately tried the experiment himself. This time, to Schibler's mystification, DBP appeared. The researchers looked at every variable, and eventually they alighted on something odd. The postdoc had performed the experiments with the rats' livers in the early afternoon. Schibler had also done his experiment in the afternoon. But the student was a farmer's son who came in around 7 A.M. and did the work in the morning.

It turned out that when the student looked for the transcription factor, it was simply not present at detectable levels. At the time, researchers generally assumed that genes made their protein products more or less consistently at all hours of the day. But the gene that made DBP was on a 24-hour cycle that repeated every day: nearly none of the protein was made in the morning, but by the afternoon, levels spiked 300-fold. Schibler and his collaborators described this surprising pattern in a second *Cell* paper published later that same year.

In the decades since, researchers from all over the world have found that genes whose expression patterns have daily highs and lows are not aberrations. In

the late 1990s researchers studying cyanobacteria, which are photosynthetic, found that more than 80 percent of the microbes' genes produce their proteins according to a circadian, or daily, rhythm. That discovery made sense because these organisms are tied so strongly to the sun, but it soon became clear that many genes in flies and mice were oscillating as well. A 2014 paper by John Hogenesch, now at Cincinnati Children's Hospital Medical Center, and his colleagues took a closer look at the phenomenon, tracing the expression of nearly 20,000 genes across 12 different tissues in mice. The team recorded gene expression levels every two hours and realized that there were rush hours when large numbers of genes became active, just before dawn and just before dusk. Furthermore, when the researchers looked at how many genes

Imagine the body as a Rube Goldberg machine, with thousands of devices whose cogs, baskets and springs must align. It turns out that not all the cogs, baskets or springs are present at any given moment.

in total had a cyclic pattern, the proportion came to a whopping 43 percent of the genome.

That study has since been cited more than 450 times, according to Google Scholar, as the trickle of papers involving circadian gene expression has become a flood. The latest estimate of genes that run by the clock in mammals, from work on nonhuman primates by Sachidananda Panda of the Salk Institute for Biological Studies in La Jolla, Calif., and his collaborators that was published in February in *Science*, is even higher: 82 percent of genes—a difference that Panda attributes in part to having sampled many more tissues in his study. "That completely changes things," Panda says. "That means there is a time aspect to the genome."

Imagine the body as a Rube Goldberg machine, with thousands of tiny devices whose cogs, baskets and springs must align correctly in a moment for life to proceed. And it turns out that not all the springs or baskets are present at any given moment. If you send a marble down a chute, the route it takes in the morning may be different from the route it takes in the evening.

The conductor of all this timed expression is the circadian clock, which is not a single object or place in the brain, as the name might lead you to believe, but a squad of about a dozen proteins. At the same time that some researchers were uncovering cycles in gene expression, others were revealing the clock side of the mystery. We now know that the clock proteins' own



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levels rise and fall over the course of the day, thanks to directions from a light-sensitive region in the brain, the circadian pacemaker. The clock proteins help to drive the expression of all the other genes that cycle daily, pushing the buttons and pulling the rods that bring some proteins into play and switch others off, regulating everything from cell division to metabolism. They are present in nearly every cell in the body.

The significance of this work is growing: The 2017 Nobel Prize in Physiology or Medicine went to three circadian clock researchers who discovered a central clock protein that builds up in cells during the night, breaks down during the day and acts as a kind of crankshaft for the whole machine. The findings of circadian clock researchers imply that on the level of the organism, there is a good time and a bad time to do anything, especially when it comes to medical intervention. But when, exactly?

POISON OR CURE?

ACETAMINOPHEN, marketed under several brand names, including Tylenol, is a danger in disguise. It is a painkiller for the most innocent of uses—headache, muscle soreness—but when too much is taken, the liver can be damaged. In a handful of days, if the overdose is not treated, the patient may die. Acetaminophen overdose is behind more than 78,000 emergency room visits a year in the U.S.

Could it be that some of acetaminophen's peculiar lethality has to do with when people take it? Chronopharmacologist Robert Dallmann of the University of Warwick in England and his colleagues have found intriguing evidence in mouse studies that the answer is yes. When you give mice a dangerously large dose in the morning, absolutely nothing untoward happens. "You give it in the evening," Dallmann says, "and the liver is basically kaput."

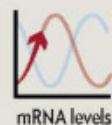
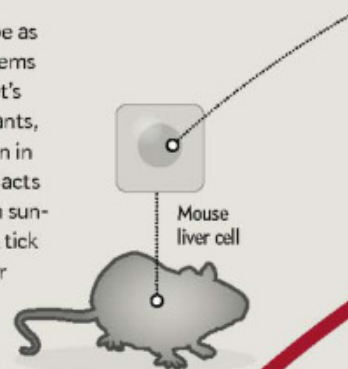
This is the way it works: As the two proteins at the heart of the clock, called CLOCK and BMAL1, go through their daily cycle in the liver, they flip a switch and cause the transcription of DBP. DBP, in turn, causes the expression of the POR enzyme. POR acts on yet another enzyme, one that pharmacologists are familiar with: CYP2E1, which is one of the liver enzymes that take apart drugs, alcohol and substances in food. Such liver enzymes ramp up their levels in the morning in humans and in the evening in mice, which are nocturnal. Schibler suggests the enzymes are being prepared for the times when the organism is most likely to eat.

POR hands off an electron to CYP2E1. If the person—or mouse—has recently swallowed acetaminophen, CYP2E1 clamps onto the drug molecule. A series of swift, small changes (moving an oxygen molecule in, executing a sleight of hand with protons and another electron) results in the release of water—and a piece of what used to be acetaminophen is now an extremely dangerous poison.

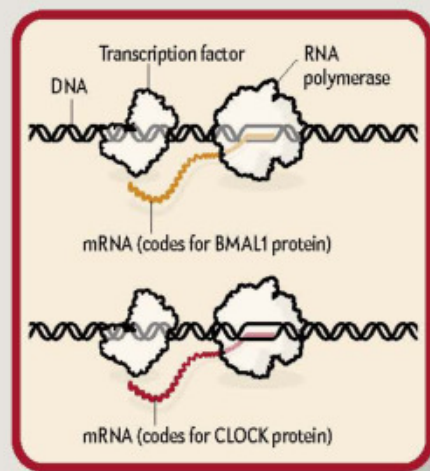
Most of the time, the poison does not stick around. As the cytochrome releases the poison, it is caught by an-

The Rhythms of a Liver Cell

Circadian clocks are ancient. They may not be as old as life itself, but various timekeeping systems that allow organisms to respond to the planet's daily cycles exist in groups as disparate as plants, bacteria and mammals. In mammals, a region in the brain called the suprachiasmatic nucleus acts as the circadian pacemaker, taking cues from sunlight. This helps to set the cellular clocks that tick in nearly every cell in the body, including liver cells (shown here). Within individual cells, two core clock proteins, BMAL1 and CLOCK, trigger the expression of many other proteins, sparking a daily feedback loop that inhibits BMAL1 and CLOCK levels before allowing them to rise once again.

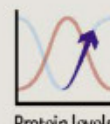


BMAL1 mRNA
CLOCK mRNA

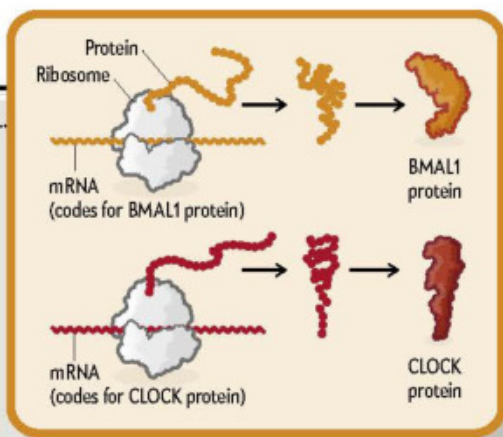


STAGE FOUR: DROP DOWN

The PER-CRY complex inhibits CLOCK and BMAL1. This means that production of PER and CRY is eventually ramped down, in a negative feedback loop. Without them, CLOCK and BMAL1 are no longer repressed, and they can be transcribed again.



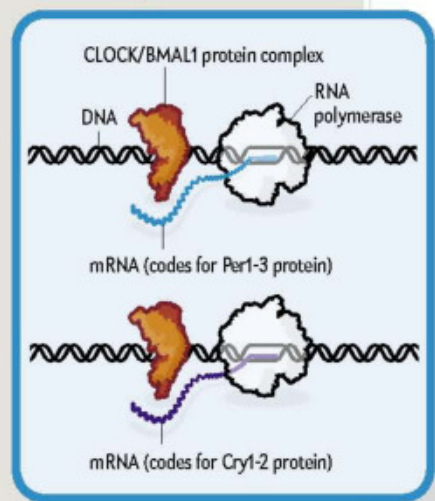
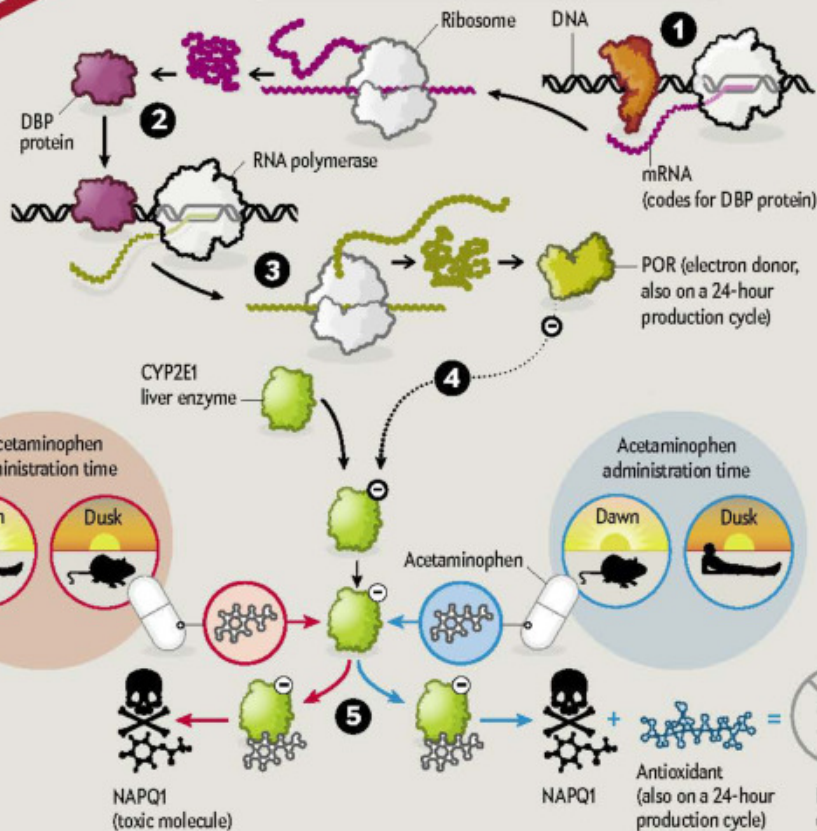
Per/Cry protein complex



STAGE ONE: WRITE THE MESSAGE

In a liver cell, the genes coding for BMAL1 and CLOCK are transcribed in messenger RNAs. Some hours later they are translated into proteins and attach to each other, forming a complex.

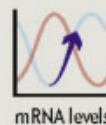
CLOCK/BMAL1 protein complex



STAGE TWO: BIND TOGETHER

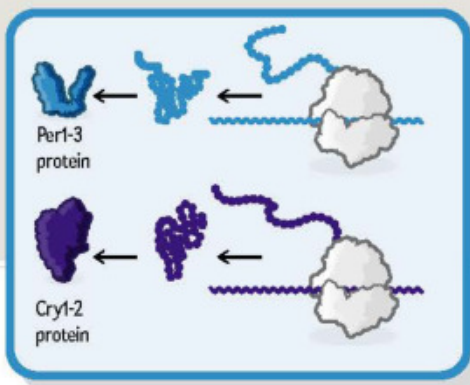
The CLOCK-BMAL1 complex attaches to the DNA, binding to promoter regions that stand in front of numerous genes. This triggers the genes' transcription into mRNAs. Among the many, many genes transcribed are two gene families called *PER* and *CRY*.

Per1-3 mRNA
Cry1-2 mRNA



WHY THE TIMING OF AN ACETAMINOPHEN DOSE MATTERS

CLOCK and BMAL1 **1** promote the transcription of DBP **2**. DBP then does the same for the POR enzyme, an oxidoreductase **3**. POR transfers an electron to CYP2E1, a liver enzyme, activating it **4**. CYP2E1 is clamped onto a newly ingested acetaminophen molecule **5** and breaks it down, releasing a toxic by-product called NAPQI. If acetaminophen has arrived when there is enough glutathione—an antioxidant that is also expressed on a 24-hour cycle to deal with NAPQI's toxicity—then NAPQI is destroyed, and all is well. If enough glutathione is not present, however, NAPQI accumulates, and disaster ensues. For mice, that danger zone is in the evening. For humans, if the biology is similar, it should be the morning.



STAGE THREE: BUILD UP

Over time the *PER* and *CRY* mRNAs are translated into proteins. These form complexes with each other and accumulate in the cell.

other enzyme and broken down into something harmless by an antioxidant. But that antioxidant also happens to be produced on a schedule set by the circadian clock. If acetaminophen arrives when the cytochrome is present and there is not enough antioxidant to handle it, the poison accumulates, and disaster ensues. For mice, that danger zone is the evening. For humans, if the biology holds the same, it would be in the morning.

Intriguingly, destroying the clock eliminates the deadly differences between morning and evening. "We can show that if we turn off the clock in the liver, this rhythm is gone," Dallmann says. In these clockless cells, genes are expressed in a more disorganized manner.

which is timing treatment for maximum safety and efficacy—have focused on some particularly dangerous drugs: those used in treating cancer. Chemotherapies can cause potent side effects and permanent harm in some patients. The biochemical processes that create these side effects have something in common with what happens to acetaminophen. Like acetaminophen, some chemotherapies can interact with liver enzymes that are under circadian control, and their efficacy sometimes seems to depend on the time of day when they are administered. Decades ago Halberg and his colleagues found that whether mice with cancer lived or died came down to the hour when they received

their medicine, relates Germaine Cornelissen of the University of Minnesota, who came to work with him shortly after.

Francis Levi, a chronobiologist and medical oncologist at the University of Warwick, and his collaborators have been performing rigorous tests of the idea for more than 20 years. In one landmark study, Levi and his colleagues looked at what happened in 93 patients with

colorectal cancer when they got their medicine at a particular time. In human cells, the enzyme dihydropyrimidine dehydrogenase is responsible for safely breaking down the chemotherapy drug fluorouracil. The enzyme's levels spike by nearly 40 percent around midnight. If patients could get their drugs then, the researchers reasoned, they might see fewer painful, dangerous side effects. Indeed, the scientists found a five-fold reduction of inflammation in the mucosal membranes and a threefold reduction in hospitalizations for side effects.

In another trial, the team found men with colorectal cancer survived longer with timed treatment, but women did not. "[The finding] does not mean that women do not benefit from chronotherapy," Levi says, "just that the timing in women has to be different from timing in men." With this particular drug, it turned out that at least in mice, the clock proteins of females cycle differently enough from those of males that the optimum treatment time was hours off. Levi and his collaborators have, with a biomedical device company, developed pumps that inject a dose at a predetermined time, even if it is when the patient or the doctors are asleep.

But if these data have been published for decades, why is chronomedicine not more widely practiced? For one thing, not all trials have seen an effect. It is hard to tell whether that is because experimenters are not looking at enough times of the day or some other variable or because there is simply nothing to be gained by timing a dose. For much of the time in which Levi and other pioneers were working on this issue, the mechanistic details of how the circadian

Will we someday go into the doctor's office knowing the details of our own clock the way we know our blood type? Will we receive a customized time card for when to take our meds?

Imagine, then, a Rube Goldberg machine that has roughly all its parts in play at once, in a kind of genetic cacophony that probably cannot be maintained for long if the animal is to stay healthy. But the mouse experiment does prove that the circadian clock is key to the effects of the drug.

CIRCADIAN INFLUENCE ON COMMON DRUGS

IF SUCH AN ENORMOUS PORTION of the genome makes proteins only at certain times of day and if drugs interact with those substances, then the time of dosing probably matters with more medications than acetaminophen. In fact, 56 of the 100 most commonly used drugs in the U.S. target rhythmically expressed proteins, Hogenesch and his colleagues reported in their 2014 paper. About half of those drugs have a half-life in the body of less than six hours, suggesting that timing the dose could make a difference in their effectiveness. Aspirin prescribed to ward off heart attacks, for instance, has only a short half-life in the body. But the enzyme it targets showed a daily cycle in heart, lung and kidney tissues in that study. Perhaps that pattern explains the results of a 2005 trial in patients with hypertension that showed that taking aspirin before bedtime lowered blood pressure, whereas taking the drug in the morning slightly elevated it. A smaller, randomized human study in 2014 showed that aspirin before bedtime caused a decrease in a kind of blood cell activity that leads to blood clots. Aspirin in the morning did not.

In addition to exploring the circadian influence on common medications, many researchers who are now interested in the idea of so-called chronomedicine—

clock functioned and exactly how it influenced what happens after you take a drug were still uncertain.

New insights may raise the field's profile. In March researchers based in China and the U.S. outlined just how the circadian clock functions in 32 different kinds of cancer. And in another recent paper, Hogenesch and his colleagues found that giving a chemo drug at the right time, when enzymes can whisk away dangerous by-products, halves its toxicity in mice.

Meanwhile mounting evidence supports the use of timed treatment for other diseases, including inflammatory and autoimmune disorders such as rheumatoid arthritis, whose sufferers have long complained of swollen, sore joints in the morning. We now know that the circadian clock is driving inflammation in the joints at that time, says Julie Gibbs of the University of Manchester in England, who studies the phenomenon. A timed-release formulation of a drug engineered to be present before waking has shown striking success in a clinical trial by another group, she says. Even the blood-brain barrier may be more permeable at certain times: Amita Sehgal and her lab at University of Pennsylvania just reported in experiments with fruit flies that seizure medications are most effective at night, because molecular pumps that remove drugs from the brain have cyclical expression.

Thanks to the snowballing number of papers on the circadian clock, this research is no longer driven by trial and error. "Efforts over the past 40 years were largely serendipitous," Hogenesch says. "We now have principled, mechanism-based strategies." In other words, researchers can plan for the fact that the body runs on a timetable.

POTENTIAL FOR PERSONALIZED MEDICINE

PHARMACEUTICAL COMPANIES and clinicians have not responded with the same level of fervor as scientists—at least not yet. Human tests of the molecular mechanisms uncovered in animals have been slow to emerge. And chronobiology is not generally studied in medical school, which means that the people who might reasonably use this information do not know much about it. From the drug companies' perspective, time of day is an expensive thing to control for. Imagine doing double the testing, just to see if morning and evening have different effects—not to mention all the times in between.

Further complicating matters, some evidence indicates that optimum dosing time can vary significantly among individuals. Although we are all running on roughly the same schedule, some people are a little slower or faster. Cornelissen and her colleagues in Japan have found that in people with high blood pressure, personalized monitoring of circadian rhythms can determine different optimum treatment times for each person. Levi's cancer studies, too, have found that studying patients' own personal daily cycle is important. This level of detail can seem bewildering.

Drug companies have already tripped over the circadian clock. Back in the 1980s, Levi says, a drug company tried to reduce the side effects of an anti-inflammatory that can cause stomach problems by introducing a delayed-release formulation. "It was a real disaster," Levi recalls. Despite all of the company's work, the rate of severe side effects did not go down. At its request, Levi ran a trial with around 500 patients and found that the drug was actually most toxic in the morning, when the new pill was designed to be taken, probably as a result of liver enzyme cycling. Checking for such effects before a drug is put on the market could be a way to avoid such snafus, as well as potentially improving efficacy.

Indeed, individual variation may not be just an inconvenience; it may also be an opportunity for pharmaceutical companies. Personalized medicine—the idea that treatment can be engineered specifically to the patient—is on the rise, and the goal of incorporating the clock dovetails with it. If one can eliminate side effects in a particular group of people by assigning them a time or giving them a formulation that only kicks in later, then that is a net benefit for a drug-maker. To that end, it is getting much easier to tell where someone is in their daily cycle with simple, noninvasive tests. Hogenesch, for instance, is currently investigating an assay using cells picked up on a cotton swab swiped across a patient's skin.

Will we someday go into the doctor's office knowing the details of our own clock the way we know our blood type? Will we receive a customized time card for when to take our meds? Answers vary, but "I really think so," Schibler says.

Because if we could go back in time to the asthmatic monk in the monastery, modern pulmonologists could explain that one reason asthma attacks tend to occur in the wee hours may be because that is when certain hormones on a circadian cycle spike. They shrink the passageways in the lungs, triggering a crisis in some people with asthma, and a drug called theophylline can reduce that effect. Today it is taken before bed in a capsule that dissolves over time so that it will be there in the blood when it is needed some hours later. More than 1,500 years after Caelius Aurelianus wrote that asthma came at night, we have some answers about time and the body—as well as new mysteries to solve. 

MORE TO EXPLORE

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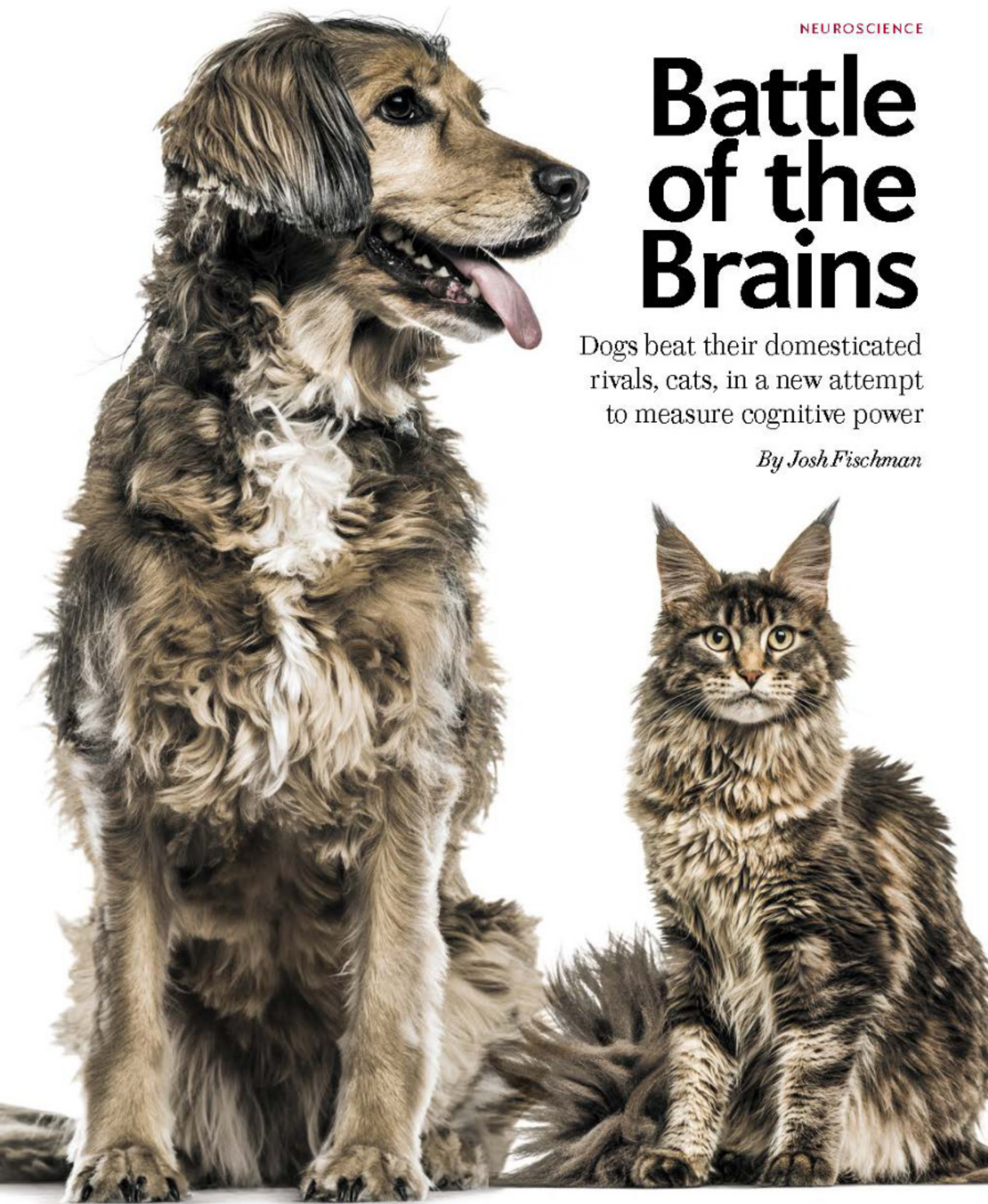
scientificamerican.com/magazine/sa

NEUROSCIENCE

Battle of the Brains

Dogs beat their domesticated rivals, cats, in a new attempt to measure cognitive power

By Josh Fischman



Adding Up Animal Neurons

A bigger cerebral cortex—or body—does not always mean more of these brain cells

A LOT OF WHAT WE THINK OF as thinking happens at the brain's outer limits. A blanket of cells, marked with deep creases, swaddles the core of the brain in every animal with a spine. This blanket integrates all kinds of information, makes decisions, interprets emotions, solves problems and creates complex behavior. It is called the cerebral cortex, and neurons in it—humans have about 16 billion—act a bit like tiny information processors to form thoughts.

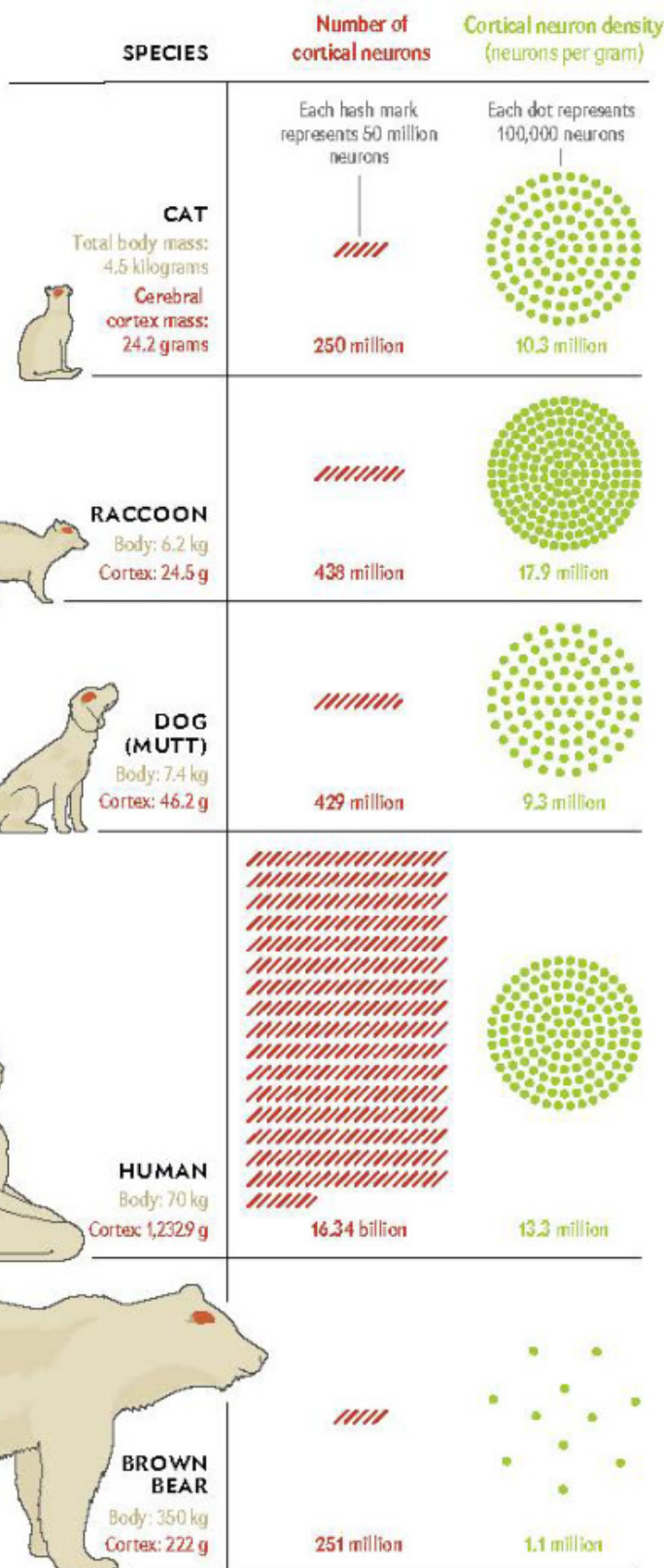
Inside the heads of our pets, a new count of these cells shows that dogs far outdistance cats. A typical mutt clocks in with almost 430 million neurons in its cortex, and a cat has just 250 million. "Dogs have what it takes to have more cognitive capability than cats," says Suzana Herculano-Houzel, a neuroanatomist at Vanderbilt University, who published the results last December in *Frontiers in Neuroanatomy*. In other carnivores, somewhat surprisingly, those with the biggest cerebral cortex are not always the ones with most neurons.

To identify and count these cells, Herculano-Houzel, working with her former graduate student Débora Jardim-Messeder and their colleagues, liquefied the cortex in a laboratory version of a blender. The result looks like unfiltered apple juice, the neuroanatomist says. ("My students say that I've ruined apple juice for them.") The scientists stirred in a probe molecule that attaches only to the nuclei of neurons in the broth, ignoring other kinds of brain cells.

They learned the raccoon has a cat-sized cortex but with almost twice as many neurons—a result that will not surprise homeowners who struggle to keep the masked creatures out of locked garbage cans. And bears turn out to be, like Winnie the Pooh, of very little brain: they have a cat-sized neuron count in a cortex that is bigger by 10-fold. Low neuron numbers seem to be a pattern in big carnivores, including lions. That maybe because large animals need a lot of energy, and neurons are energy hogs. They require a lot of nutrients, so "we would expect animals to have as few neurons as needed, since they come with a high cost," says anthropologist Evan Maclean, director of the Arizona Canine Cognition Center at the University of Arizona. If a brawny body can help an animal survive, it might not need as much brainpower.

As for cats and dogs, Maclean says, cortical neuron counts may not mean one can be called "smarter," because cognition can take many forms and involve other brain areas. He does note that there is some evidence dogs hang on to information longer than cats do, which may be related to cortical capability. Herculano-Houzel, who owns two dogs and has heard from unhappy cat owners about her conclusions, emphasizes that "you should love your pet no matter how many neurons are in the cortex."

Josh Fischman, a senior editor at *Scientific American*, wrote about a coral reef's fight for survival in the December 2016 issue.





HIGH-VOLTAGE WIRES extend from a transmission tower, as seen from below.



ENERGY

BUILD ING A WEATHER- SMART GRID

Renewable energy will rule only when weather data drive the design of a new electric grid

By Peter Fairley

Peter Fairley is a freelance writer in Victoria, B.C., who specializes in energy and the environment.



THE WIND POWER BOOM IN THE PACIFIC NORTHWEST'S COLUMBIA RIVER GORGE IS BOTH A RENEWABLE energy success story and a cautionary tale. Engineers packed the gorge with thousands of wind turbines that power two million to three million homes. The carbon-free energy, however, regularly causes migraines for operators at the Bonneville Power Administration, based in Portland, Ore., who manage the regional electricity grid. Changing weather shifts winds across the broad span of turbines, creating huge power swings. The havoc is multiplied by Mount Hood, which towers over the gorge and divides the prevailing winds like a big boulder in a stream. The wake from the split meanders through the gorge's wind farms, causing output to spike and slump. For Bonneville, it is akin to a big nuclear power plant on a dimmer switch, with power swinging up and down.

Managing the grid is even more dicey in the spring, when power output surges from the Northwest's massive hydroelectric plants. The dams need to operate flat out because the reservoirs behind them are brimming with meltwater. Spilling water over the wall without generating power would waste the potential energy while filling the river with excess air and killing endangered salmon hatching there by "giving them the bends," says Justin Sharp, a Portland-based energy consultant. So Bonneville sometimes shuts down the wind farms, squandering some of their clean energy.

Sharp knows this situation well because he helped create it. After earning his Ph.D. in meteorology by studying the region's rich winds, he spent seven years at energy developer Iberdrola Renewables (now Avangrid Renewables) mining that resource with turbines, which currently feed Bonneville's grid. Sharp says developers designed the wind farms for maximum annual output at lowest cost, and Bonneville beefed up transmission lines to carry that output to market. But everyone, he adds, ignored the weather and climate variability. "Did we assess that variability when we were thinking about building those wind farms? No. Do we assess it now? No. Does it have an impact on the system and its ability to manage lots of wind? Absolutely. A huge amount."

The same story is repeated across the U.S. Experts such as Sharp peer ahead to a day of reckoning for states, cities and businesses planning to switch to carbon-free electricity. If builders

continue to ignore weather-driven variability, future grids will become increasingly precarious. "We're trying to ram the square peg of renewables into the round hole of the existing electric system, and I think we're heading for a train wreck," Sharp says.

What is needed is weather-smart grid design, directed by meteorology and built on long-distance transmission lines that can manage the weather's inconsistencies. Such a system could ship gobs of renewable power across North America to link supply with demand, whatever the weather throws at it—allowing, for example, surplus wind in the Columbia River Gorge to help Minneapolis keep humming when Midwestern winds stall, and vice versa. "We haven't done that yet," says Charlie Smith, executive director of Energy Systems Integration Group, an industry association dedicated to managing variable power generation.

TAMING MONSTERS

TO BE FAIR, weather has always informed grid design but only to a crude degree, says Aaron Bloom, who manages the Grid Systems Analysis Group for the U.S. Department of Energy's National Renewable Energy Laboratory (NREL) in Golden, Colo. Heat waves and cold snaps produce the peak strain on a region's grid. Typical planning boils down to ensuring the system can deliver during those hairiest hours of the most extreme weather days. But the rapid scale-up of wind and solar power plants is forcing planners to greatly boost the grid's weather smarts, Bloom says.

IN BRIEF

Wind and solar power will not become the major energy sources until a nationwide transmission grid is designed based on local, daily weather variations.

Models that use detailed weather data can optimize the siting of renewable energy sources and direct-current power lines to connect them.

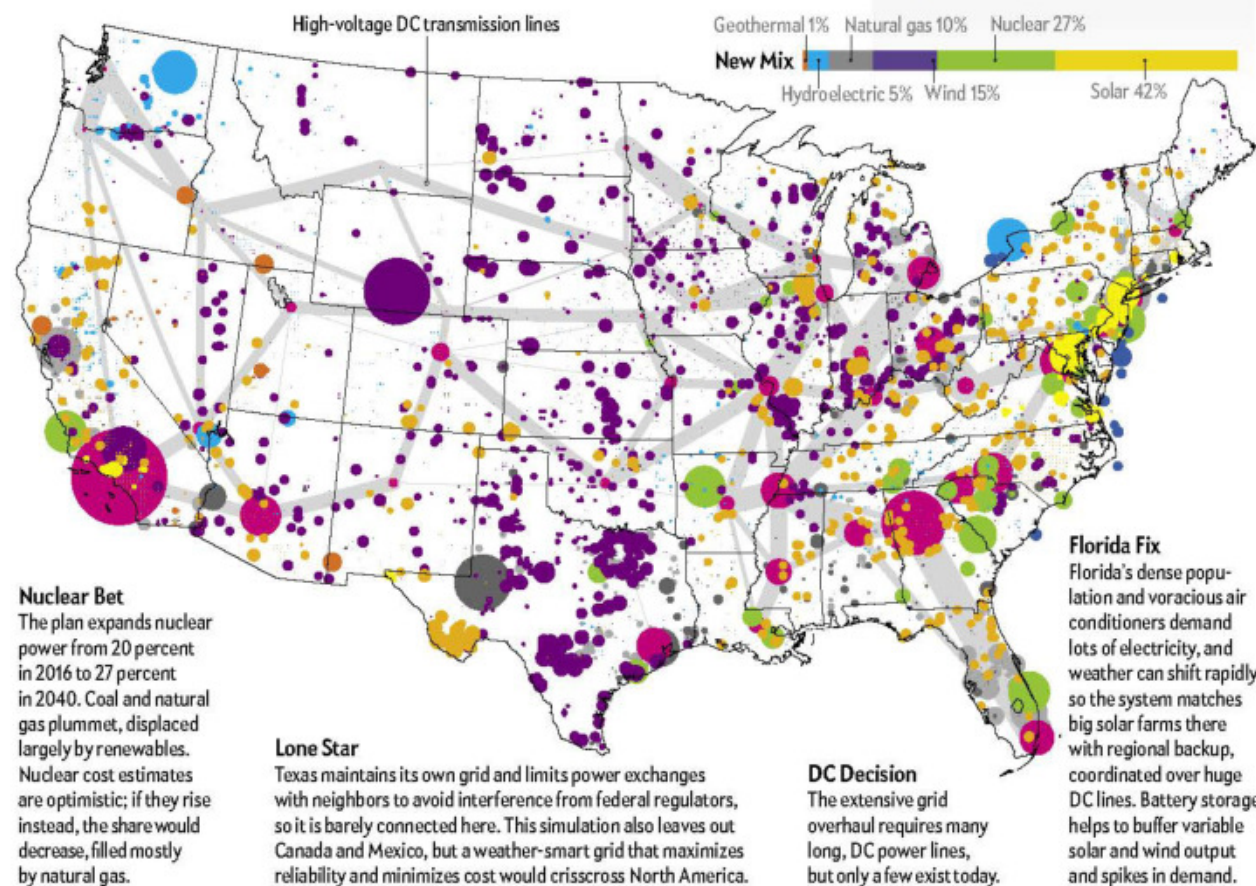
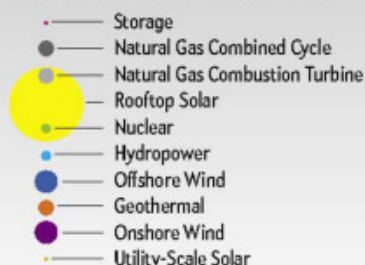
One model raises renewables to 67 percent of the U.S. electricity supply. But resistance by states and power firms to long DC lines has stifled weather-smart grids.

Power Makeover

Radically redesigning the U.S. power system could boost renewable electricity to more than 67 percent of supply by 2040 and eliminate coal plants. The configuration here would emit 89 percent less greenhouse gas than the 2016 system and trim electric bills by 10 percent. The key is using detailed data about how weather changes in every three-by-three-kilometer square of the country every five minutes, year-round, to determine which power plants to build where (dots) and how to most efficiently connect regions with direct-current transmission lines (gray). This plan, by Vibrant Clean Energy, uses more widely distributed plants than today, so they can back up one another as weather changes nationwide.

Idealized Power Plan for 2040

Each dot represents one type of local power source. Each dot size below represents 1,000 megawatts. On the map, larger dots are proportionally more; smaller are less.



Unlike conventional coal, natural gas and nuclear generators, wind turbines and solar panels strongly react to the weather, adding a big variable that changes every day of the year.

Texas and California illustrate the challenge. Texas leads the U.S. in wind capacity, with more than 20 gigawatts installed. But the prevailing winds blow hardest at night, dumping an energy surplus on the grid, thereby forcing utilities to actually pay big customers to take it. That sounds crazy, but it can be less costly than turning the wind systems off and wasting the energy.

California has ample wind and leads the nation in solar power plants and photovoltaic rooftops. The solar collectors raise an electrical tsunami every morning when the sun comes up—sometimes more than the grid can absorb—and then give out in the early evening when consumers still demand plenty of power. California has little recourse. “They’re a north-south state, so the sun rises and sets

at much the same time on every solar panel,” says Mark Ahlstrom, vice president of renewable energy policy for NextEra Energy Resources, a project development company focused on renewables. Extreme weather, meanwhile, disrupted both states’ wind power supplies three winters ago. An unusually stable high-pressure ridge over the West Coast cut winds to record lows for several months.

States often get little help from the rest of the country because the grid across the U.S. is divided into three big, isolated regions. This balkanization means each region must manage weather variability on its own. The Eastern Interconnection and Western Interconnection—the two alternating-current (AC) power grids that serve most of the U.S. and Canada and a bit of Mexico—exchange almost no power. And they exchange even less with Texas, which operates its own AC grid.

Consumers are unaware of the mounting drama renewables

may cause because giant wind turbines and solar arrays supply only 7.6 percent of U.S. electricity, combined. Grid operators still have thousands of conventional power plants they can ramp up and down to balance these gyrating sources. But renewables' share is headed skyward. California has mandated that it will reach 50 percent by 2030 (not including large hydropower plants); Hawaii intends to hit 100 percent as soon as 2040. Only a few utilities and transmission operators are trying to design weather-wise grids to handle the coming flood of wind and solar power. But a growing set of design tools are rising to the challenge.

BIG WEATHER DATA

BLOOM'S TEAM AT NREL, and outside experts such as James McCalley of Iowa State University, is wrapping up a major study that is evaluating the benefits of expanded power sharing between the Eastern and Western grids. The Interconnections Seam Study is the first to employ new wind and solar data sets that have extremely fine spatial and temporal resolution, taking simulations to a new level. NREL's data provide snapshots of weather and power flows nationwide for every five-minute interval during an entire year, mapping wind on every two-square-kilometer patch of land and solar on every four-square-kilometer patch. Such detail is crucial for charting wind power variability over complex terrain, such as the Columbia River Gorge. Projecting wind speed at multiple heights also enables NREL to select an optimal turbine technology at any site. The results of all those smarts are simulations that demonstrate how to cost-effectively and reliably boost renewable supply in the continental U.S. (minus Texas) to more than 54 percent by 2040—far greater than today's level.

The simulations erase the Eastern-Western power divide by knitting the two grids together along their common border with several big direct-current power lines or by crisscrossing them with a network of longer DC lines from the Pacific Coast to the Midwest, plus a main line from Louisiana to Florida. DC wires are used because they lose much less power than AC wires do over long distances, making faraway delivery economically viable. NREL's models determined how much power the lines should be able to carry and where to place new generators to take advantage of the bolstered transmission system.

The models recognize various opportunities for weather-smart optimization, such as installing a greater range of wind turbine types and solar panels in more widespread locations rather than bunching them in a few exceptionally windy or sunny regions, where they tend to get located today. The result is very likely more consistent renewable energy requiring fewer reserves by conventional power plants, according to NREL energy modeler Greg Brinkman. "Natural diversity gets baked in," he says.

NREL's modeling, for all its sophistication, also shows the enduring challenge of weather-smart design. For example, McCal-



WIND FARMS in Washington State could send electricity thousands of miles eastward if the U.S. power grid were upgraded with DC lines.

ley made several simplifications to keep each simulation run to a "tractable" six or seven days of computing. And the modeling step that assigns renewable generators to specific locations used a simplified temporal and spatial picture rather than five-minute-interval and four-square-kilometer precision.

The laboratory also prefixed the start and end points for the DC wires to avoid what Bloom calls a "mathematically intractable" calculation. As a result, the model did not always optimize generators and transmission routes simultaneously. Still, preliminary results from NREL show that long DC wires would save \$3.8 billion annually by, for example, slashing coal and gas consumption, paying for themselves more than three times over. But each kilometer of DC transmission could deliver even greater savings—and deeper cuts in carbon emissions—with a fully optimized layout.

Recent modeling to redesign Europe's grid for the robust renewable energy expected there by 2040 confirms that NREL's simulation shortcuts most likely leave some renewable energy potential on the table. The European Network of Transmission System Operators for Electricity, a Brussels-based consortium, added enough wind, solar and other renewable generators to a 2030 grid model to boost total renewables to 75 percent. Its experts then produced a conceptual 2040 grid by expanding interconnections between countries to alleviate bottlenecks in seasonal power flow. Finally, they redistributed the same generators to take better advantage of the redesigned grid. This iterative process of optimization boosted renewable energy to more than 80 percent in the 2040 design.

BETTER ALGORITHMS

ONE INDEPENDENT RESEARCHER claims he can merge all these modeling techniques together to squeeze even more value from the

INCK SPENCE/Getty Images

weather data. Christopher Clack, CEO of Vibrant Clean Energy, a grid-modeling and power-forecasting firm in Boulder, Colo., developed his advanced weather-driven grid algorithms during a four-year stint at the National Oceanic and Atmospheric Administration. Then, in 2016, he launched his proprietary, commercial software, called WIS:dom.

WIS:dom uses the same kind of high-resolution weather data that NREL does but in a different way, Clack claims, and thus creates more opportunities for renewable energy. His recent analysis of the big U.S. grids led to a system in which renewables would provide 62 percent of generation by 2040, which is 20 percent more than NREL's most recent projection. The simulated grid also delivers power 10 percent cheaper than today's. Clack says his model could push renewables to more than 67 percent, long before 2040, if the savings were plowed back into accelerated investment in the transmission system.

Clack argues that WIS:dom squeezes more intelligence from weather data by simultaneously optimizing power plants and transmission—notably the long DC lines—rather than fixing the lines ahead of time, as NREL had to do. The model also taps into how renewable generators across the country tend to fluctuate relative to one another hour by hour, better balancing wind and solar power in distant places. For example, WIS:dom can tell when Texas's rising nighttime wind energy can offset lagging offshore winds on the East Coast, which blow more during the day. "All the different regions help other regions at different times," Clack says. NREL's model, with its restrictions, may miss some of this, McCalley acknowledges, although he questions whether the simplifications make much difference.

Clack says his model takes "only" two days of computing to spit out the more optimized grid plans. Experts say his integrated models may be a breakthrough in weather-smart design. "He definitely has taken it to a higher level of fidelity," Ahlstrom says.

What WIS:dom lacks, however, is validation. Experts such as Ahlstrom, Bloom and others wish they knew more about how Clack's proprietary tool works so they could confirm its reliability. "Chris is a smart guy. He's doing some great stuff. I just don't know what his special sauce is," Bloom says. It seems unlikely that Clack will be sharing it. He is, after all, selling outputs from his software to energy companies, including advice on where regional grid operators and entrepreneurial transmission builders should target billions of dollars in investments.

POLITICAL INHIBITORS

ENERGY DEVELOPERS such as Sharp and Smith are trying to encourage grid companies and scientific organizations such as the American Meteorological Society to emphasize weather-smart planning. They also say political and industry leaders must campaign for DC transmission to overcome resistance to it. State renewable energy mandates are prompting grid operators to build AC lines to reach wind and solar resources. But only a handful of firms are trying to build the long DC lines needed to exchange renewable energy among regions, as Europe, China and others are doing.

Not-in-my-backyard opposition to power lines is part of the problem. Another is a shift in utility investments toward "non-wire" solutions for grid issues, such as battery storage. Big, expensive batteries located where power is needed can accept surplus power—such as from the Texas night winds—and save it for a few dark, windless days. But batteries may do little to help regions

endure extreme events such as the 2015 Western wind drought. "It's not like you're going to be able to take all of that power that your [solar] is generating during the summer and put it into a battery for the winter," Sharp says.

Regional turf wars may be an even bigger barrier to long DC interconnections. Local and state officials have often blocked large power lines carrying cheap energy from afar to protect in-state generators. The resistance to big DC has been a bitter lesson for Dale Osborn, who led the team that designed the NREL study's DC network. Osborn was the U.S. power industry's leading advocate for DC-enhanced grids until he retired last year from the Midcontinent Independent System Operator, which operates the power lines and a wholesale power market shared by 15 U.S. states and Manitoba. As NREL's analysis shows, a system that can trade electricity from Washington State to Florida requires fewer power plants across the country. Although this approach reduces overall cost, "there are a lot of self-serving people who don't want lower-cost generation," Osborn laments. "They want higher prices for *their* generation."

Clack says high-voltage DC (HVDC) prospects look so dim in the U.S. that clients typically ask him to exclude it from the studies he performs for them, forcing WIS:dom to make do with shorter, more numerous AC lines. "The long-distance HVDC is turned off because most believe it will not happen," Clack says—at least not for the foreseeable future. And unfortunately, he notes, when he turns DC off yet keeps costs constant, roughly half of the carbon dioxide emissions reductions that result from fewer conventional power plants vanish.

The federal government could help break the gridlock. President Barack Obama's secretary of energy, Ernest Moniz, exercised untested statutory authority to take land through eminent domain for a DC line deemed to be of national importance. That undertaking, designed to move surplus wind power from Oklahoma to markets in the mid-South and Southeast, was recently put on the back burner by its proponent, Clean Line Energy Partners, while it fights for several projects in the Midwest that were also stalled by local and state opposition.

Similar transmission activism under President Donald Trump is less likely. Secretary of Energy Rick Perry is focused on protecting coal-fired power plants, arguing that expanding their on-site coal reserves makes the grid more "resilient" against extreme weather. But experts point out that coal piles can freeze during cold snaps and flood during tropical storms, forcing the plants to shut down. The same weather often brings atmospheric pressure gradients that spin wind turbines and clear skies that maximize solar output. As Sharp observes, "There are places within the country with very robust renewable energy during extreme weather."

If only there was a weather-smart grid to deliver it. 

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BUZZ KILL

As mosquito-borne diseases spread, scientists are fighting back with new poisons, traps and genetic engineering techniques

By Dan Strickman

IN BRIEF

Mosquitoes are responsible for more than 725,000 deaths annually, which makes them the deadliest creatures on the planet.

Climate change and globalization are exacerbating the threat the insects pose, and mosquitoes are developing resistance to common insecticides.

Vector-control experts are fighting back with new tools ranging from low-tech traps to genetic-modification schemes.





Dan Strickman is a medical entomologist, who heads up vector-control operations at the Bill & Melinda Gates Foundation.



H

UMANS HAVE BEEN LOCKED IN A STRUGGLE with disease-carrying mosquitoes for most of recorded history. With just two bites—one to pick up a pathogen and another to transmit it—the bugs have fueled countless outbreaks.

Malaria exploded across Africa as humans first gathered for agricultural development. Yellow fever nearly wiped out Memphis, Tenn., in the 1870s as urbanization and river transport brought infected people and mosquitoes together. Some archaeologists suspect that mosquito-borne disease even hastened the fall of the Roman Empire.

hands of other humans annually. In parts of the world where people are exposed to the bugs during much of the year, including sub-Saharan Africa and swathes of South America and Asia, mosquitoes cripple economic growth. All told, the bugs are responsible for killing more people than all the wars in history combined.

It once seemed like we would defeat mosquitoes. In 1939 Paul Hermann Müller discovered that a colorless, tasteless synthetic substance called dichlorodiphenyltrichloroethane, better known as DDT, was an excellent bug killer. The powerful chemical was applied to many homes, farms and

The Bill & Melinda Gates Foundation, where I head up vector control, now puts the death toll from mosquitoes at around 725,000 people a year. By comparison, 475,000 humans die at the

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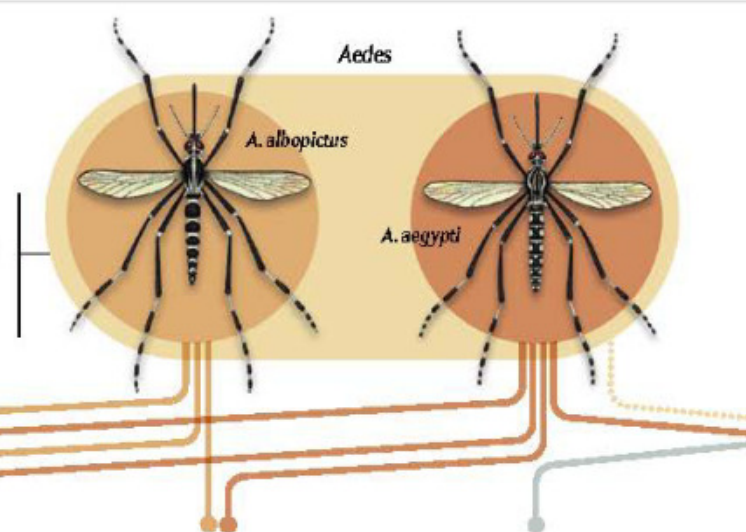
PHOTOGRAPH BY GETTY IMAGES

Tiny Critters, Big Impact

Of the 3,500 species of mosquito found worldwide, only a small fraction cause the most illness and suffering.

Major Players

Certain species of mosquito are capable of carrying a raft of diseases—at the same time. The *Aedes aegypti* mosquito, for example, lives in the same areas as half the world's population, and it can transmit Zika, dengue, chikungunya and yellow fever.



CHIKUNGUNYA

SYMPTOMS: Fever, joint pain, headache, muscle pain, rash

FAST FACTS: Before 2013, scientists did not detect any local transmission of the virus in the Americas. But last year there were more than 123,000 cases of confirmed local transmission there.

DENGUE

SYMPTOMS: Fever, severe headache, severe eye and joint pain, rash, low white cell count

FAST FACTS: Before 1970, only nine countries had experienced serious dengue epidemics. The disease is now endemic in more than 100 countries.

ZIKA

SYMPTOMS: Often asymptomatic, but it can cause fever, rash, headache

FAST FACTS: Recently caused a multiyear global public health emergency; can be transmitted via mosquito bite or sex or passed from mother to fetus. Causes grave birth defects, including microcephaly.

MALARIA

SYMPTOMS: Fever, chills, sweats, headaches, nausea, vomiting

FAST FACTS: Malaria deaths reached 445,000 in 2016, with most cases and deaths occurring in Africa. That year 91 countries reported a total of 216 million cases.

military bases, accomplishing the miracle of eliminating malaria in some of the areas hardest hit by the disease. Müller was awarded a Nobel Prize in 1948 for his lifesaving work. But this insecticide came with unknown consequences for human health and a steep cost to the environment. The chemical accumulated in fish, plants and the fatty tissue of mammals, wreaking havoc throughout the food chain. When certain birds, including bald eagles, ospreys and falcons, ate DDT-contaminated fish, the exposure weakened their eggs, and as a result their populations fell to alarming levels. By the early 1970s DDT use was severely restricted, and mosquitoes—and malaria—soon flourished once again.

In recent decades climate change and globalization have combined to exacerbate the mosquito threat, making mosquito-borne disease an increasingly common problem in myriad settings, including the U.S. Last year about 2,000 people contracted West Nile virus in the U.S. In the past five years chikungunya virus—which causes severe joint pain—spread to 45 countries, causing more than two million reported cases, including multiple large outbreaks in the U.S. territories. And although only 21 cases of Zika have occurred in the U.S. in 2018 at the time this article went to press—all among travelers returning from Zika-affected areas—the virus is still a problem in many parts of the world. In all, more than 47,000 cases of human illness caused by mosquito bites were reported throughout the U.S. and its territories in 2016; a decade earlier there were fewer than 7,000.

The best mosquito-control strategies home in on specific mosquito species that carry diseases and kill enough of them to disrupt transmission. Yet increasingly it has become clear that our existing weapons are failing: mosquitoes have developed

resistance to many of the insecticides that we place on bed nets to ward off malaria, and as the spread of Zika in recent years has shown, it is incredibly difficult to effectively kill off certain species of mosquitoes, such as *Aedes aegypti*, that live in our homes and can breed in tiny pools of stagnant water.

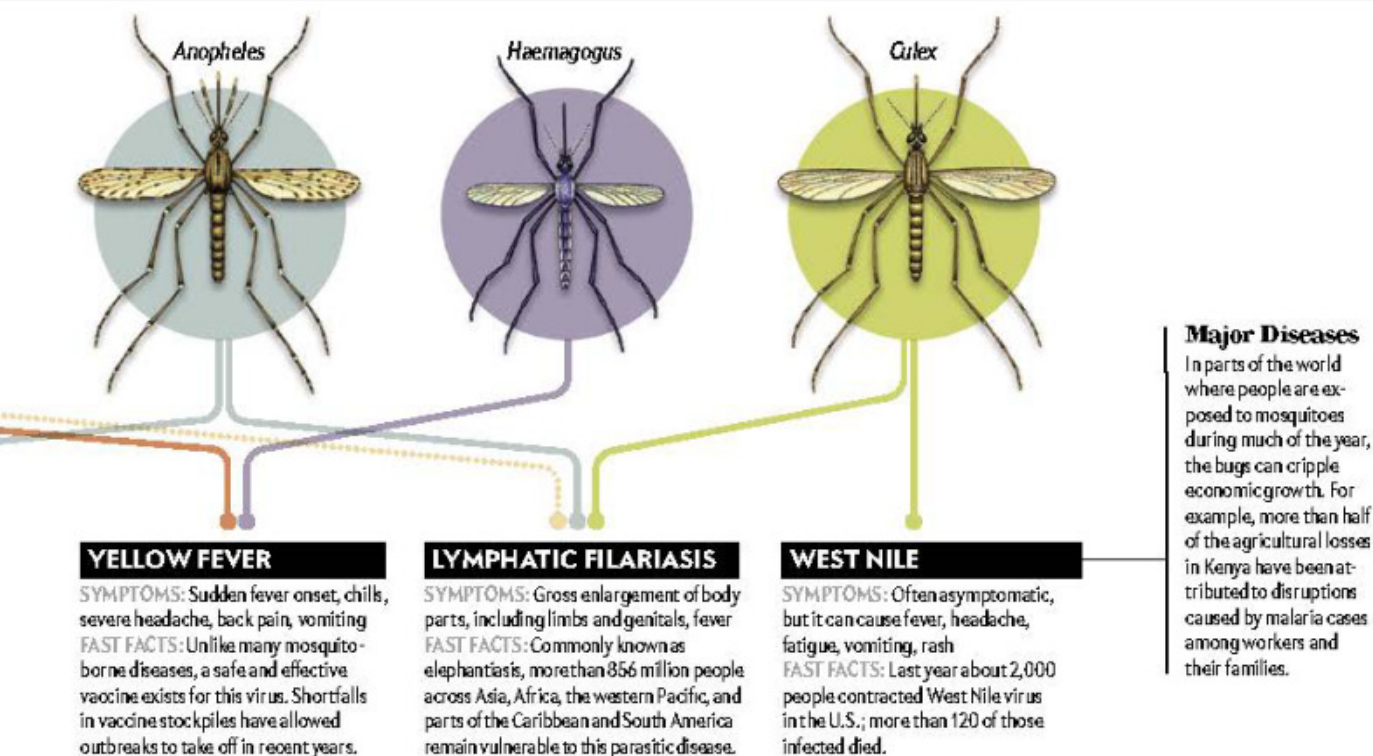
To counter this trend, scientists in dozens of countries have been working to develop new tools for mosquito control: improved insecticides, better traps, and even schemes to use radiation or gene manipulation to render mosquitoes sterile. The ideas underpinning some of these tools are sometimes decades old. Yet technical advances, investments by many groups, including ours, and widespread acceptance that mosquito control is an inherent part of disease control are finally putting this approach back on the map.

A BETTER TRAP

OF THE DISEASES SPREAD by mosquitoes, malaria has proved particularly intransigent and deadly. In 2016, 216 million people were sickened by malaria worldwide, 445,000 of whom died. Certain species of *Anopheles* mosquitoes are carriers for the malaria-causing *Plasmodium* parasite. When female mosquitoes bite humans—seeking the nutrients they need for their eggs—the bugs may unwittingly pick up these parasites. (Male mosquitoes do not bite.) *Plasmodium* then reproduce in the mosquito's gut before they travel to the bug's salivary glands. About a week later, when the mosquito feeds again, the parasite hitches a ride in the bug's spit to a new human host, ultimately infiltrating that person's liver and bloodstream and causing sickness or death.

The disease's wide reach and alarming death toll have netted

RESEARCH BY AMANDA ROBES



it the biggest and best-funded mosquito-control efforts. In 2016, \$2.7 billion was spent on malaria research and elimination. Yet the greatest obstacle is often pinning down *where* the control should be applied—finding ways to wipe out the bugs in their environment while minimizing harm to nearby humans and wildlife. Enter eave tubes. The small gap between the roof and the top of the exterior wall in most tropical houses is called an eave. Mosquitoes find human prey in many ways, including following a person's carbon dioxide output through the eaves in their house. In the past few years researchers have started to roll out eave tubes that simultaneously close off those openings and help to reduce malarial transmission. An eave tube is a simple, safe device consisting of a plastic tube and an electrostatic screen dusted with insecticide powder. The tubes transform entire homes into mosquito traps with humans as the bait. When mosquitoes try to enter the home through the tube, they land on the insecticide-coated screen and die.

Researchers have been testing eave tubes in the field for close to a decade. Preliminary unpublished results from a 2016–2017 field trial in Ivory Coast, conducted by Pennsylvania State University in cooperation with European and African partners, indicate that in homes where eave tubes were installed malaria transmission in children may have been cut by as much as 40 percent. The hope is that eave tubes will eventually replace indoor residual spraying—a technique that works well but is more difficult to apply and requires more insecticide. Eave tubes are also safer for kids; the poison is located too high up for them to reach. Moreover, the approach can help minimize the growth of insecticide resistance. As the bugs try to wriggle through these small openings, the powder coats the whole body with a much larger dose than when the bugs briefly land on a surface treated with insecticides, making it more likely the tubes will kill their target.

Not all mosquitoes feed indoors, however, and not every house is suitable for eave tubes. To fight those bugs, Israeli scientists have been developing insecticide-laced sugar baits that attract both male and female mosquitoes. The baits deliver massive doses of poison compared with other traps designed to kill adult mosquitoes because mosquitoes think the poison is sugar they need to survive; a mosquito will imbibe about 20 percent of its body weight in the sweet bait. The bugs consistently fly up to the bait product (which is about the size of a standard sheet of printer paper) and bite through a sheath that contains small chambers of poison-laden bait. Field experiments in Mali have shown that the sheath membrane's tiny openings allow mosquitoes and other insects adapted for blood feeding to access the poison while keeping it out of reach for pollinators such as bees.

Researchers reported at a recent tropical medicine conference that when they hung two traps on the outside of each home in a Malian village, almost half of the malaria-carrying mosquitoes in that immediate area consumed the poison. (To count mosquitoes, researchers caught a sampling of the bugs and examined their guts for signs of the colored dyes that the poison bait had been laced with—a sign that would confirm the



IN MALI, workers from the University of Bamako's Malaria Research and Training Center check on a sugar-bait mosquito trap.

mosquitoes had visited the traps and consumed the poison.) As a result of their intervention, about 90 percent of female mosquitoes in that area—the only sex that bites humans—died shortly after their poison meals, before they were able to transmit malaria via their bites.

MOSQUITO BIRTH CONTROL

RATHER THAN KILLING MOSQUITOES, what if we could prevent them from ever being born? One plan, spearheaded by the United Nations' International Atomic Energy Agency, is to release male mosquitoes sterilized by exposure to ionizing radiation, which harms cellular growth and development in the testes. The idea is that these laboratory-grown sterile insects will mate with wild females, producing eggs that will never hatch. Because most females mate only once in their life, this method could substantially decrease mosquito populations.

In a separate U.N.-supported project run by the Tropical Medicine Research Institute in Sudan, lab workers are mass-producing sterile *Anopheles arabiensis* mosquitoes—the most prevalent malaria vector in the country—in a special rearing facility for future release. The project is still at the testing stage, but there is reason to be optimistic. In the early 1950s American entomologist Edward Knippling set out to use the same approach—known simply as the sterile insect technique—with the New World screwworm fly, a pest that lays eggs on wounds in livestock and humans that later hatch into flesh-eating maggots. It took decades, but by 2006 the screwworm fly had been eliminated from North and Central America, saving the livestock industry billions of dollars a year.

Similarly, sterilization offers the possibility of a nearly permanent area-wide solution to the mosquito problem with minimal ongoing maintenance work. Yet it requires a lot of organization and infrastructure without much possibility of financial profit; therefore, it has mostly been explored by governments rather than by private enterprise.

Private companies, energized by new interest in mosquito control following the Zika crisis, are hoping that a different

type of sterilization effort will prove to be a faster, easier and more thorough way to take out mosquitoes. In these schemes, scientists manipulate the genetics of the bugs themselves. For example, to help Brazil get rid of the mosquitoes that transmit dengue and Zika, a private company called Oxitec has been releasing genetically engineered mosquitoes into the wild—mosquitoes that have been bred in the lab to pass on a gene that kills female offspring. The genetically altered mosquitoes go on to mate with wild mosquitoes, rapidly spreading the trait in a population. During an experimental release of these lab-grown mosquitoes in a suburb of the city of Juazeiro in northeastern Brazil, the number of *A. aegypti* mosquitoes there fell by 95 percent within nine months. Two other Brazilian cities have also reported successes with the mosquitoes. But this work remains controversial, and critics say there are lingering questions about unintended environmental consequences.

Genetically driven sterilization efforts could take years to work on any significant scale, but there is another option. Researchers at Imperial College London contend that we should employ “gene drive” tools to quickly push specific genetic changes through the mosquito population. The best way to control malaria, they explain, is to use gene-editing tools such as CRISPR to introduce a specific gene into individual bugs and then “drive” that change throughout an entire population. The CRISPR-editing system is encoded into an embryonic insect’s DNA, ensuring that the trait is preferentially passed on to its offspring. Theoretically, after many generations, the entire population will have that gene—overriding the natural rules of inheritance in which sexually producing organisms have a 50–50 chance of inheriting a gene from each of their parents because scientists make the desired change on both chromosomes.

For malaria control, that altered genetic information could either change the mosquitoes so they could not transmit malaria, disrupt the sex ratio in the next generation or simply kill the next generation of bugs. There are clear similarities to the radiation- and gene-based sterile insect techniques, but gene drive would potentially work with far fewer mosquito releases because the modified genes would spread throughout the population within several generations of its introduction.

Yet gene drive, too, is also controversial because of concerns about unforeseen consequences. As a result, thus far no community field trials have gotten the green light. Some scientists who work in the field have also said that wild mosquito populations will develop resistance to gene drives over time—something that has already occurred in lab experiments—and could ultimately render this approach ineffective. Such resistance could arise in a number of ways. In one, natural genetic variation could alter the short genetic sequences that gene-drive systems would otherwise target. Alternatively, cellular repair processes may alter target DNA sequences so that a gene-drive system can no longer recognize them.

THE DANGER OF REINTRODUCTION

ELIMINATING ALL MOSQUITOES is a fantasy. In the U.S., the most effective abatement districts spend from about \$1 to \$10 per person per year to spray insecticides, remove standing water and clear mosquito-friendly vegetation—yet even that does not completely get rid of them. Killing all mosquitoes could also disrupt food chains and plant pollination in ways we do not

even suspect. Besides, only a couple of hundred of the 3,500 mosquito species scientists have identified bite humans and carry diseases, so it would also be overzealous to obliterate them all. The best we could hope for, and probably the only option that would be environmentally safe, would be to eliminate some of the key species from specific areas.

I believe we could achieve that. In Haiti, for example, perhaps we could kill off the main malaria-transmitting species with the sterile male technique while protecting people against other disease-carrying mosquito species with effective eave tubes and sugar-bait traps. We would also need to preemptively monitor human patients and the local mosquito population for signs of emerging threats and tamp down any small outbreaks that may arise. With such comprehensive strategies, it is not unimaginable that within five years the parasites that cause malaria would be gone from the entire island.

Even then, however, there would still be a danger of reintroduction. History demonstrates that if a ship of infected people arrives in a previously disease-free area—or worse, a mosquito species capable of carrying the disease from Africa or Southeast Asia—maladies such as malaria can resurface. Although the worldwide trend has been to free countries from malaria, there are at least 68 documented examples of resurgence of the disease in communities following a reduction in mosquito control. The *A. aegypti* mosquito managed to make a comeback in Brazil in the 1980s after DDT spraying ceased there, for example. As a result, dengue and yellow fever reappeared in the nation, and chikungunya and Zika viruses cropped up, too. When DDT spraying stopped in India, because of shortages of the chemical and other factors, malaria returned there as well.

We have never had so much innovation or funding in the area of mosquito control. Private foundations such as ours, government agencies and the World Health Organization are collectively spending about \$570 million annually on dedicated malaria research, whereas in 2002 the annual spending levels were closer to \$100 million. But even with the aid of new tools, mosquito control requires constant vigilance. Mosquito problems are seldom solved permanently and must be attended to constantly—just like any other public health hazard. 

Editors' note: The Bill & Melinda Gates Foundation financially supports several of the discussed projects, including aspects of eave tubes, sugar baits and gene drive.

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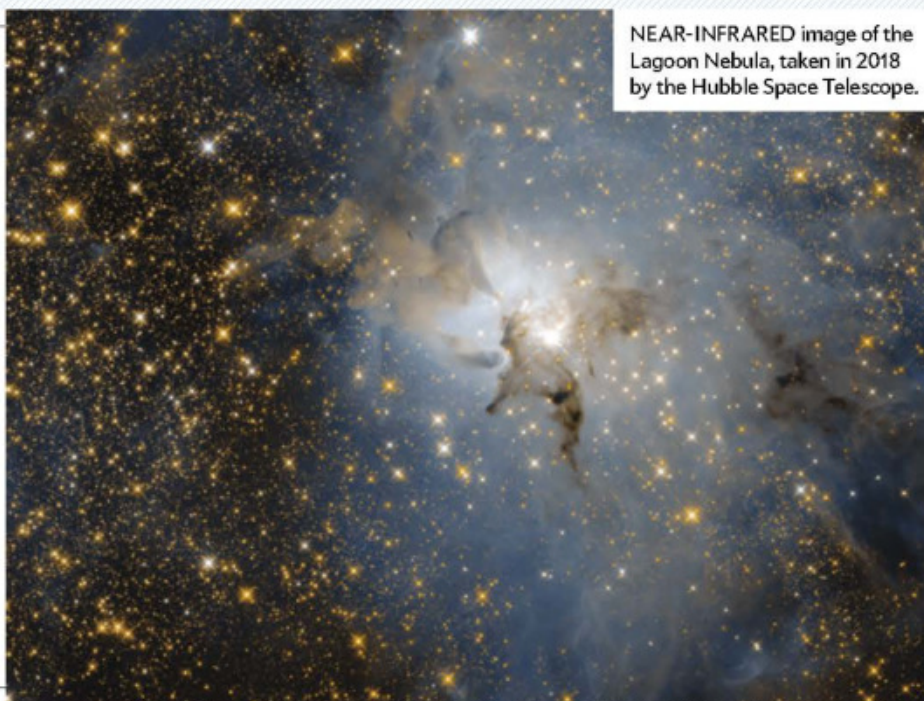
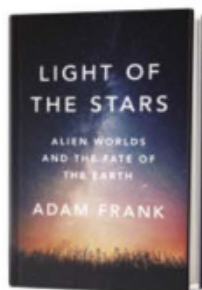
The Dengue Stopper. Scott O'Neill; June 2015.

scientificamerican.com/magazine/sa

Light of the Stars:

Alien Worlds and the Fate of the Earth

by Adam Frank.
W. W. Norton,
2018 (\$26.95)



NEAR-INFRARED image of the Lagoon Nebula, taken in 2018 by the Hubble Space Telescope.

Though once an aid for agriculture and navigation, astronomy—the study of the heavens above—is now often seen as disconnected from life on Earth, an academic pastime with scant value for human beings. Frank, an astrophysicist, combines his expertise with findings from planetary science, ecology, and more to show that lessons from distant stars and alien worlds could help humanity grapple with climate change, nuclear war and other existential threats. Studies of Venus, for instance, have revealed how Earth's climate can and will change in the future, and investigations of Martian dust storms were a major basis for the concept of “nuclear winter.” Future studies of habitable planets beyond our solar system—or even the technological civilizations they might harbor—could offer further untold benefits. *Light of the Stars* provides a marvelous perspective on how astronomy could make us all better Earthlings.

—Lee Billings

Troublesome Science:

The Misuse of Genetics and Genomics in Understanding Race

by Rob DeSalle and Ian Tattersall. Columbia University Press, 2018 (\$35)



Genetically, race is a meaningless concept, yet our society seems far from ready to stop dividing people into racial categories. Evolutionary biologist DeSalle and paleoanthropologist Tattersall

debunk the idea as a useful scientific classification, explaining how the technique of taxonomy—the grouping of organisms based on shared characteristics—fails to find significant genetic differences among the groups we commonly call races. They bemoan the fact that they have to keep rehashing the debate (this is their second book on the topic). “As science, race may (or should) be a dead issue,” they write, “but it shows zombie-like tenacity on the social and political fronts.” —Clara Moskowitz

The Darker the Night, the Brighter the Stars: A Neuropsychologist's Odyssey through Consciousness

by Paul Broks. Crown, 2018 (\$27)

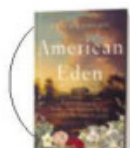


What are we? How should we live? Such questions have occupied humans since the dawn of consciousness. Motivated by the grief of his wife's death,

neuropsychologist and writer Broks weaves a mesmerizing web of memories, his own research, Greek mythology and the writings of famous philosophers to muse on the nature of awareness. The scientific underpinnings of how our brain functions are just the start, he says—for example, several of his clinical cases link specific regions of the brains to certain types of thought; beyond that, the workings of the mind are at once random, staggering and bewildering. “If we are to get anywhere close to understanding consciousness, the first thing to acknowledge is its absurdity,” Broks writes.

American Eden: David Hosack, Botany, and Medicine in the Garden of the Early Republic

by Victoria Johnson. Liveright, 2018 (\$29.95)



In the fall of 1797 the eldest son of Alexander Hamilton, Philip, fell ill with yellow fever, which was sweeping through New York City. The family doctor,

David Hosack, employed an unorthodox treatment of hot baths of Peruvian bark and alcohol and saved the boy's life. As sociologist Johnson documents, Hosack went on to establish the nation's first botanical garden—the Elgin Botanic Garden—in the place that is now Rockefeller Center and to launch the American era of botany. He used the Elgin collection to conduct some of the earliest methodical research on the medicinal properties of plants, including poppies from which opiates are derived and the two plants that would later be involved in the development of aspirin.



Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com) and a Presidential Fellow at Chapman University. His new book is *Heavens on Earth: The Scientific Search for the Afterlife, Immortality, and Utopia*. Follow him on Twitter @michaelshermer

The Final Mysterians

Are consciousness, free will and God insoluble mysteries?

By Michael Shermer

In 1967 British biologist and Nobel laureate Sir Peter Medawar famously characterized science as, in book title form, *The Art of the Soluble*. "Good scientists study the most important problems they think they can solve. It is, after all, their professional business to solve problems, not merely to grapple with them," he wrote.

For millennia, the greatest minds of our species have grappled to gain purchase on the vertiginous ontological cliffs of three great mysteries—consciousness, free will and God—without ascending anywhere near the thin air of their peaks. Unlike other inscrutable problems, such as the structure of the atom, the molecular basis of replication and the causes of human violence, which have witnessed stunning advancements of enlightenment, these three seem to recede ever further away from understanding.



even as we race ever faster to catch them in our scientific nets.

Are these "hard" problems, as philosopher David Chalmers characterized consciousness, or are they truly insoluble "mysterian" problems, as philosopher Owen Flanagan designated them (inspired by the 1960s rock group Question Mark and the Mysterians)? The "old mysterians" were dualists who believed in non-material properties, such as the soul, that cannot be explained by natural processes. The "new mysterians," Flanagan says, contend that consciousness can never be explained because of the limitations of human cognition. I contend that not only consciousness

but also free will and God are mysterian problems—not because we are not yet smart enough to solve them but because they can never be solved, not even in principle, relating to how the concepts are conceived in language. Call those of us in this camp the "final mysterians."

Consciousness. The hard problem of consciousness is represented by the qualitative experiences (qualia) of what it is like to be something. It is the first-person subjective experience of the world through the senses and brain of the organism. It is not possible to know what it is like to be a bat (in philosopher Thomas Nagel's famous thought experiment), because if you altered your brain and body from humanoid to batoid, you would just be a bat, not a human knowing what it feels like to be a bat. You would not be like the traveling salesman in Franz Kafka's 1915 novella *The Metamorphosis*, who awakens to discover he has been transformed into a giant insect but still has human thoughts. You would just be an arthropod. By definition, only I can know my first-person experience of being me, and the same is true for you, bats and bugs.

Free will. Few scientists dispute that we live in a deterministic universe in which all effects have causes (except in quantum mechanics, although this just adds an element of randomness to the system, not freedom). And yet we all act as if we have free will—that we make choices among options and retain certain degrees of freedom within constraining systems. Either we are all delusional, or else the problem is framed to be conceptually impenetrable. We are not inert blobs of matter banded about the pinball machine of life by the paddles of nature's laws; we are active agents within the causal net of the universe, both determined by it and helping to determine it through our choices. That is the compatibilist position from whence volition and culpability emerge.

God. If the creator of the universe is supernatural—outside of space and time and nature's laws—then by definition, no natural science can discover God through any measurements made by natural instruments. By definition, this God is an unsolvable mystery. If God is part of the natural world or somehow reaches into our universe from outside of it to stir the particles (to, say, perform miracles like healing the sick), we should be able to quantify such providential acts. This God is scientifically soluble, but so far all claims of such measurements have yet to exceed statistical chance. In any case, God as a natural being who is just a whole lot smarter and more powerful than us is not what most people conceive of as deific.

Although these final mysteries may not be solvable by science, they are compelling concepts nonetheless, well deserving of our scrutiny if for no other reason than it may lead to a deeper understanding of our nature as sentient, volitional, spiritual beings. ■

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Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 36 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.



Sex and Drugs

Animals' inner lives are stranger than we can imagine

By Steve Mirsky

Drug lord Pablo Escobar died in 1993. But his legacy lives on. For example, more than 40 hippopotamuses roam free in Colombia, stemming from a handful that wandered away from his private zoo. It's the largest population outside Africa.

Natural history filmmaker and author Lucy Cooke mentioned what have been dubbed the "cocaine hippos" on a recent visit to New York City from her home in London. She was in town to talk about her new book *The Truth about Animals: Stoned Sloths, Lovelorn Hippos, and Other Tales from the Wild Side of Wildlife*.

Cooke rounds up tales of 13 species—her "menagerie of the misunderstood." Some animals have a bad reputation to this day based on medieval texts, including bestiaries, which "mixed up fact with folklore and a lot of morality," Cooke remarked.

Our still negative image of hyenas may date back to the salacious conclusions moralists drew from the animals, before more open-minded field researchers realized that the larger individuals were actually females sporting what is called a pseudo penis.

On the other modified forelimb, penguins do that humanlike upright walk and have a tight-knit family structure that led conservative commentators to laud the 2005 documentary *March of the Penguins*, Cooke said, for its display of "models of Christian family values." But, she continued, "unfortunately, penguins are birds with little, tiny brains ... and they're programmed to have

sex with anything that moves and quite a lot of things that don't move, like dead penguins."

Moving slightly faster than the dead are sloths. The first Spaniards to see them were not impressed. Cooke quotes the conquistador Oviedo, who wrote that the animal was "the stupidest thing that can be found in the world." But he was looking at a specimen sprawled on the ground. "Gravity removes its dignity," Cooke said. When enjoying its evolved arboreal lifestyle, however, the sloth is a genius. It's "an incredibly energy-efficient way to exist," she added. "All you need to have is strong hands to hook on and hang They require [significantly] less muscle than most mammals, so they burn much less energy."

The endangered pygmy three-toed sloth lives only on a small island off Panama, where it eats leaves "believed to contain alkaloids with a property similar to Valium," Cooke writes in her sloth chapter. Hence the stoned sloths of her subtitle.

Speaking of drugs, Escobar had kangaroos, zebras, giraffes, rhinos and other exotic living booty, in addition to the starter set of four ornery hippos. "One male ... nicknamed *El Viejo*—'the old man'—and three females," Cooke explained. When Escobar

violently bought the farm, most of the animals were sent to zoos and other facilities that could care for them properly.

"Apart from the hippos," which, she noted, were too massive to be moved. They "couldn't have been happier." In Africa, they face challenges of drought, competition and predation on their young. "Whereas in Colombia, the hippos have got all the rain all year-round, verdant fields to graze in, no hippos to compete with and no predators. So the population of Pablo's hippos just went boom."

Rivers in Colombia serve as what Cooke called "hippo super-highways," making it easy for hormonally active young males kicked out of the group by the jealous *El Viejo* to quickly find a new home. But the hippo harem lifestyle means that females stay close to home. And so intrepid explorers won't find female companionship, leaving them "sexually frustrated Lotharios," aka lovelorn.

Possibilities for population-control plans include killing the invaders, which many hippo-liking Colombians are against. After all, hippos are charismatic enough to get Jada Pinkett Smith to voice one in the *Madagascar* films. But they are actually quite dangerous—being hit by a charging hippo is like getting run down by a 1973 Cadillac Fleetwood doing about 30 mph.

Or "Plan B, which was a radical castration program." But "hippos have internal testicles." And they can retract when grabbed by forceps. A castration is thus long, expensive and potentially perilous. Looks like we'll eventually find out how expensive it is to have an ever growing population of hungry, hungry hippos cruising down the rivers of South America. Looking for love. ■

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JULY

1968 Heart Attack Specialists

"The development of coronary care units promises a profound change in the treatment of patients with coronary artery disease. These units, although small and unpretentious facilities within a hospital, seldom exceeding eight beds, constitute a major therapeutic innovation in dealing with the inordinate mortality from heart attacks. Each year more than 1.5 million Americans suffer coronary attacks, and of these about 600,000 die. A person who suffers a heart attack and who is taken to a hospital that lacks a coronary care unit has no better chance for survival today than a person so stricken 30 years ago."

X-ray Crystallography

"A culmination of sorts has been reached in the past few years with the successful structural analysis of several of the basic molecules of living matter—the proteins—each of which consists of thousands of atoms held together by an incredibly intricate network of chemical bonds. The most recent success has been hemoglobin (by [Max Ferdinand] Perutz); the model of this protein contains 10,000 atoms. I confess that when I contemplate one of these models, I can still hardly believe that it has been possible to work out all its details by the optical principles of X-ray analysis, which half a century ago claimed sodium chloride as its first success. —Sir Lawrence Bragg" Bragg shared the 1915 Nobel Prize in Physics with his father, William Henry Bragg, for x-ray crystallography.

1918 October Surprise

"In the enormous concentration of gun fire on the western front we have a reminder of the foul treachery of Trotzky [sic] and Lenine [sic], when these two

German agents told the simple peasant soldiers of Russia to abandon the lines, since the war was over. They did so, leaving behind them along seven hundred miles of Russian front no one knows how many thousands of guns, big and little. This war material is now on the western front taking its toll of lives, French, British, and American. These two German agents also succeeded in handing over to Germany a whole fleet of warships, many of them among the latest and most efficient types, but we do not know how far the crazy revolutionists may have allowed the fleet in commission to deteriorate."

1868 Drain the Swamp

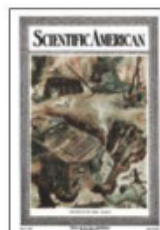
"The draining of swamp lands is not a new idea. Pumping, ditching, and the erection of dikes or levees are only partially successful. Water percolates through such artificial embankments; the rats and land crabs soon destroy



1868: Two workmen "chisel" a trench for an iron plate to help drain swamps in New Jersey.



1968



1918



1868

their integrity. The iron dike invented by Mr. S. B. Driggs, of New York, seems to put an effectual barrier in the way of these destructive agents. It is constructed by driving iron plates into the soil and joining them end to end. The weight of workmen, or blows upon the tops with stones, is sufficient in very soft mucky soils, while when the turf is too tough and unyielding, it is cut by a process called chiseling [see illustration]."

The Wonderful Brain of Phineas Gage

"Nearly twenty years ago the medical journals of the world recorded a most singular case of a laborer in Cavendish, Vt., who while engaged in blasting had a tamping iron blown entirely through his head but who actually recovered within sixty days. Such a surprising and unprecedented result was generally disbelieved, many eminent surgeons pronouncing it a physical impossibility, but the subsequent public exhibition of the individual himself, convinced the most skeptical, and verified the first report of Dr. John M. Harlow, the attending surgeon who published the case. At a very recent meeting of the Massachusetts Medical Society, this gentleman read a paper giving a history of the case, and presented the veritable skull which sustained the injury. The man's general health appears to have been good until 1859. He was taken with epileptic fits which finally caused his death in May, 1861, almost 13 years after the accident. The effect of the injury upon the man seems to have been the destruction of the equilibrium between his intellectual faculties and the animal propensities. He became capricious, fitful, irreverent, vacillating, impatient of restraint, a child in mind, an adult in physical system and passions."

Mental Illness Overlap

A distinct set of genes may underlie several psychiatric conditions

People who have autism, schizophrenia and bipolar disorder may have different challenges, but the ailments might arise from a common set of genes. Researchers compared genetic analyses of 700 human brains from deceased individuals who had one of those three disorders, major depression or alcoholism (*columns*) with brains of individuals who had none of the conditions. They examined 13 groups of genes thought to function together (*rows*). The scientists found that five groups had a pattern of overactivity or underactivity across at least three of the five conditions (*blue and gray panels*). Bipolar disorder, for example, was more similar to schizophrenia than to major depression even though clinicians may link bipolar disorder and depression, based on their symptoms. These insights could possibly reveal new treatments, says neurogeneticist Daniel Geschwind of the University of California, Los Angeles, one of the investigators. He adds that one path to that result, which has not yet been tested, could be to “put the different groups of genes in lab dishes and see which drugs reverse any overexpression or underexpression of the genes.”

How to Read This Graphic

Each column is a psychiatric condition. Each row is a group of genes that typically act together in the brain.

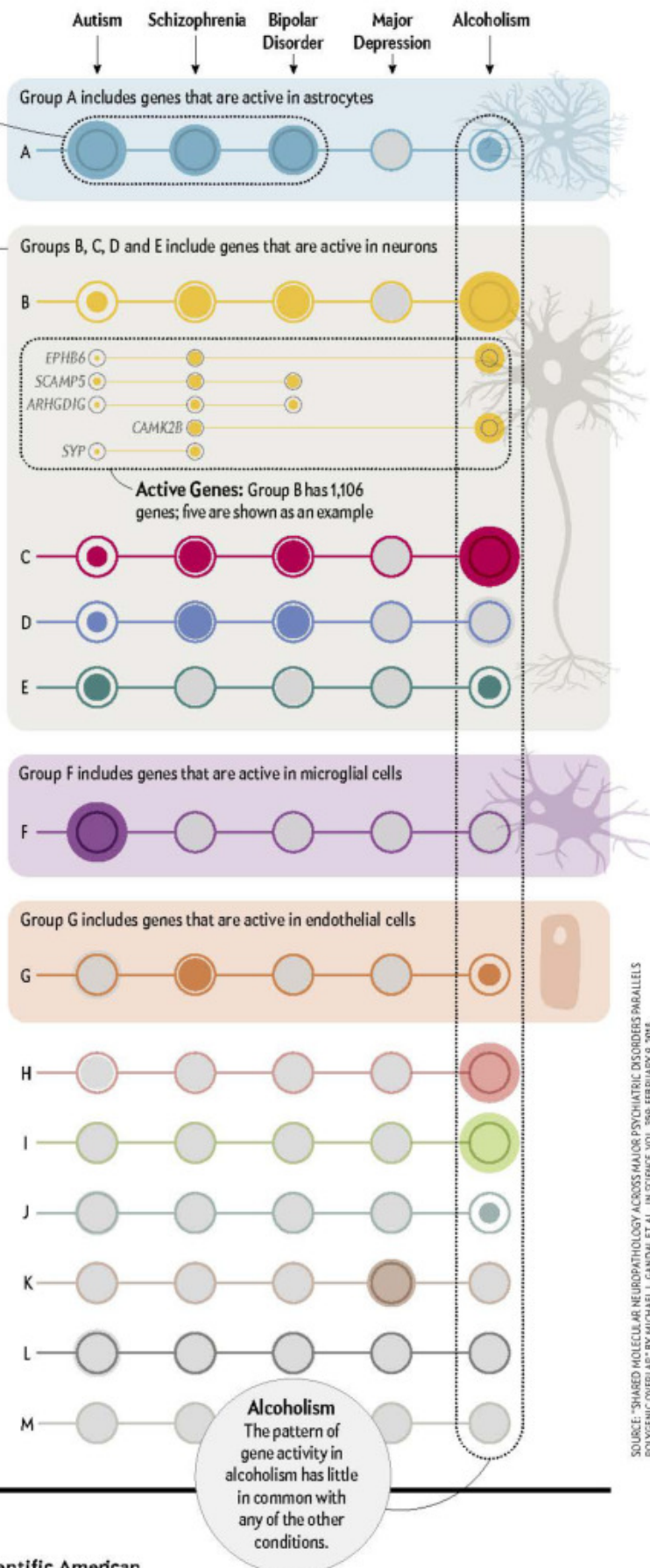
Circle size reflects level of gene expression compared with brains that had no disorder.



Gene Groups: Certain genes in the brain tend to work as a preferred unit and together become more or less active in particular types of brain cells, such as astrocytes, neurons, microglia or endothelia. Researchers identified 13 groups (*rows A–M*). Each one might have between 100 and 1,100 genes. Groups in rows H–M show no preference for any cell type.

Hyper Genes
One group of genes prevalent in a type of brain cell called an astrocyte is overactive in autism, schizophrenia and bipolar disorder.

Common Pattern
Three groups of genes (B, C, D) in brain neurons are underactive in autism, schizophrenia and bipolar disorder. Yet two of the four are overactive in alcoholism.



SOURCE: “SHARED MOLECULAR NEUROPATHOLOGY ACROSS MAJOR PSYCHIATRIC DISORDERS PARALLELS POLYGENIC OVERLAP,” BY MICHAEL I. GANDAL ET AL., IN *SCIENCE*, VOL. 359, FEBRUARY 9, 2018



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